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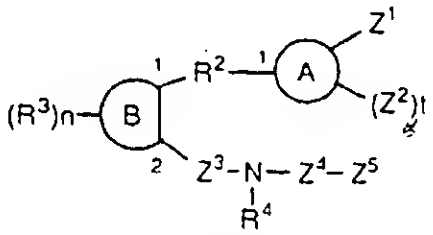
(54) SULFONAMIDE AND CARBOXAMIDE DERIVATIVES AND DRUGS CONTAINING THE SAME AS THE ACTIVE INGREDIENT

(57) The sulfonamide or carboamide derivatives of the formula (I) and a pharmaceutical composition which comprise them as an active ingredient:



(I)

(wherein A ring, B ring is carbocyclic ring, heterocyclic ring; Z^1 is -COR^1, -CH=CH-COR^1 etc.; Z^2 is H, alkyl etc.; Z^3 is single bond, alkylene; Z^4 is SO_2, CO; Z^5 is alkyl, phenyl, heterocyclic ring etc.; R^2 is $CONR^8$, O, S, NZ^6, Z^7-alkylene,

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(Cont. next page)

alkylene etc.; R^3 is H, alkyl, halogen, CF_3 etc.; R^4 is H, (substituted) alkyl etc.; n, t is 1-4).

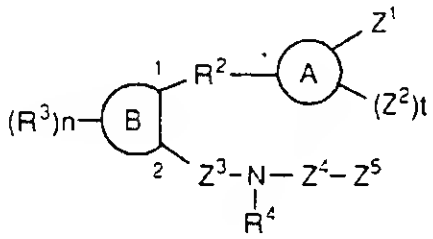
The compounds of the formula (I) can bind to receptors of PGE_2 and show antagonistic activity against the action thereof or agonistic activity. Therefore, they are considered to be useful as medicine for inhibition of uterine contraction, analgesics, antidiarrheals, sleep inducers, medicine for increase of vesical capacity or medicine for uterine contraction, cathartic, suppression of gastric acid secretion, antihypertensive or diuretic agents.

Descripti n

Field of technology

[0001] This invantion reletes to sulfonemide and carboamide derivatives. More particularly, this invention relates to

(1) the compounds of the formula (I)



(I)

(wherein all symbols are as hereinafter defined.),
(2) processes for preparing tham and
(3) Prostaglandin E_2 (abbreviated as PGE_2) antagonists or agonists which comprise them as an active ingredient.

Background

[0002] PGE_2 has been known es metabolite in the arachidonete cascade. It has been known thet PGE_2 causes uterine contraction, induction of pain, promotion ot digestive peristalsis, awakening effect, vesica contraction, suppression of gastric acid sacretion or reduction of blood prassure etc. The PGE_2 antagonist or PGE_2 agonist is expacted to show the tollowing actions.

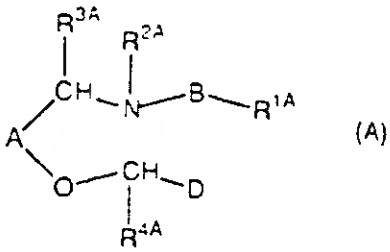
[0003] To entegonize egainst PGE_2 means to suppress the effects ebove mentioned, so such an activity is linked to inhibition of uterine contraction, analgesic action, inhibition of digestive peristalsis, induction of sleep or increase of vesical capacity. Tharefore, PGE_2 antagonists are considered to be useful tor the prevention of abortion, as analgesics, as antidiarrheals, es sleep inducers or es agents for treating pollakiuria.

[0004] To show PGE_2 agonistic activity means to promote the effects above mentioned, so such an activity is linked to uterine contraction, promotion of digestive peristalsis, suppression of gastric acid secretion or reduction of blood pressure or diuresis. Therefore, PGE_2 agonists are considered to be useful as abortifacient, cathartic, antiulcer, antigastritis, entihypertensive or diuretic egents.

[0005] A lot of PGE_2 agonists including PGE_2 itself etc. have been known, but only a few compounds (PGE_2 antagonists) possessing the inhibition of activity ot PGE_2 by antagonizing against PGE_2 hava been known.

[0006] For example, the patent applications relating to PGE entagonists are as follows:

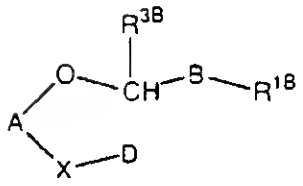
[0007] In the specificetion of WO-96/03380, it is disclosed that the compounds of the formule (A)



(A)

(wherein A is phenyl which may be substituted etc., B is ring system which may be substituted, D is ring system which may be substituted, R^{1A} is carboxyl etc., R^{2A} is H, C1-6 alkyl etc., R^{3A} is H, C1-4 alkyl, R^{4A} is H, C1-4 alkyl (as axcerpt).) are active as PGE antagonists.

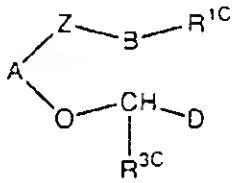
[0008] In the specification of WO-96/06822, it is disclosed that the compounds of the formula (B)



(B)

(wherein A is ring system which may be substituted, B is hetero aryl ring which may be substituted or phenyl which may be substituted, D is ring system which may be substituted, X is $(CHR^4)_n$ or $(CHR^4)_pCR^4{=}CR^4(CHR^4)_q$, R^{1B} is carboxyl etc., R^{3B} is H, C1-4 alkyl, R^4 is H, C1-4 alkyl (as excerpt).) are active as PGE antagonists.

[0009] In the specification of WO-96/11902, it is disclosed that the compounds of the formula (C)

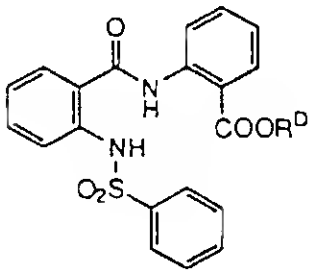


(C)

(wherein A, B and D are various ring systems, R^{1C} is carboxyl etc., R^{3C} is H, C1-4 alkyl, Z is $-(CH(R^5))_m$ etc. (as excerpt)) are active as PGE antagonists.

[0010] On the other hand, some compounds having a similar structure to the present invention compounds have been known.

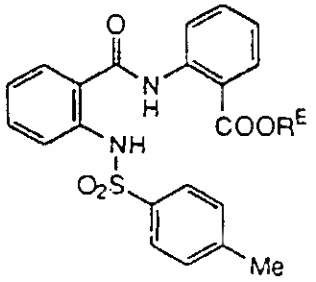
[0011] For example, the following compound is described in Justus Liebigs Ann. Chem. (1909), 367, 133.



(D)

(wherein R^D is H or ethyl)

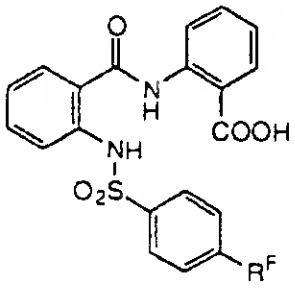
[0012] The following compound is described in Khim. Geterotsikl. Soedin (1974), (6), 760.



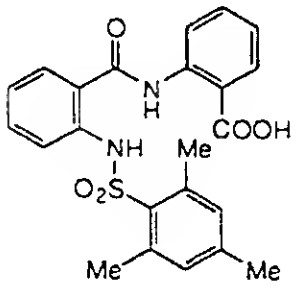
(E)

(wherein R^E is phenethyl, benzyl, hexadecyl, decyl, nonyl, butyl, propyl, ethyl, methyl.)

[0013] The following compound is described in Khim. Geterotsikl. Soedin (1972), (10), 1341.



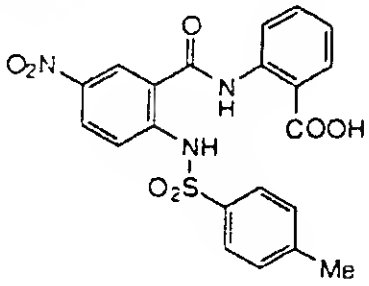
(F-1)



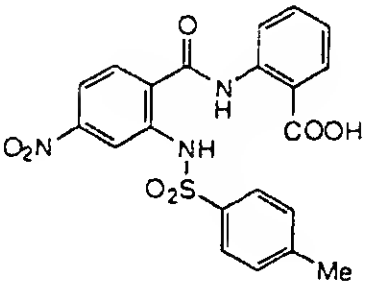
(F-2)

(wherein R^F is nitro or methoxy.)

[0014] The following compound is described in Khim. Geterotsikl. Soedin (1972), (5), 616.

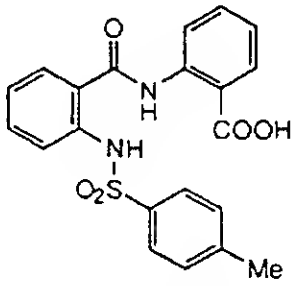


(G-1)



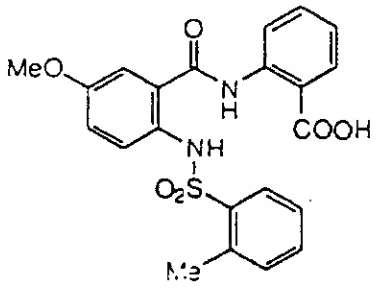
(G-2)

[0015] The following compound is described in Khim. Geterotsikl. Soedin (1976), (5), 641.

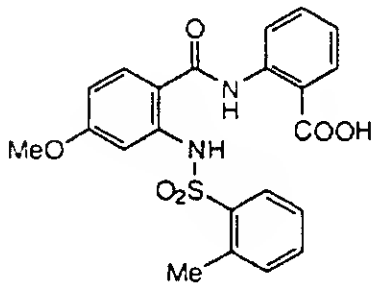


(H)

[0016] The following compound is described in Khim. Geterotsikl. Soedin (1971), (7), 1028.

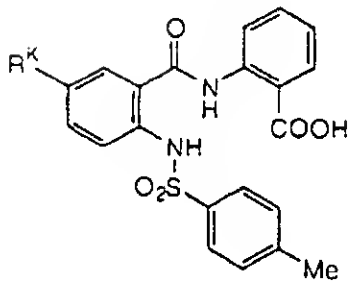


(J-1)

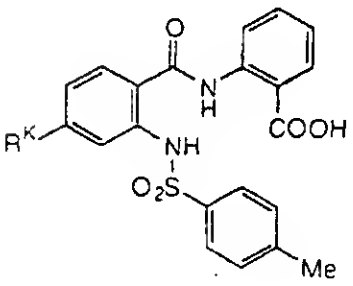


(J-2)

[0017] The following compound is described in Khim. Geterotsikl. Soedin (1970), (12), 1597.



(K-1)



(K-2)

(wherein each R^K is Br or Cl.)

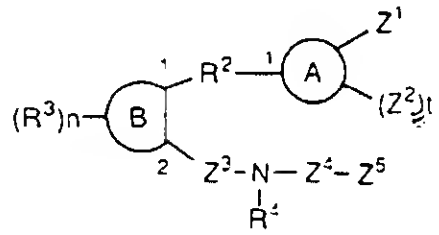
[0018] The compounds of the formula (A), (B) and (C) in the related arts possess the same pharmacological activity as the present invention compounds. But there is a difference in structure as follows: The present invention compounds have sulfonamide or carboamide as en essential element in their structure. On the other hand, the compounds described in such related arts have ether or alkylene in the corresponding part. So, it is not easy to predict the present invention compounds from the structure of these related arts.

[0019] In addition, the compounds of the formula (D) to (K) relate to the study for synthesis only. In these literature, there is no description on pharmacological activity. The carboxyl group in such compounds is connected at the ortho position, so the present invention compounds are different from such compounds in structure. Therefore, it is not easy to predict the present invention from such compounds possessing the different activity and structure.

The Disclosure of the Invention

[0020] The present invention relates to

(1) sulfonamide or carboamide derivatives of the formula (I)



(I)

(wherein

end

each, independently, is C5-15 carbocyclic ring or 5-7 membered heterocyclic ring containing one or two oxygen, sulfur or nitrogen atom(s),

Z^1 is

-COR^1,
-C1-4 alkylene-COR^1,
-CH=CH-COR^1,
-C≡COR^1, or
-O-C1-3 alkylene-COR^1
(wherein R^1 is hydroxy, C1-4 alkoxy or formula

$$NR^6R^7$$

(wherein R^6 and R^7 each, independently, is H or C1-4 alkyl.).), or
-C1-5 alkylene-OH,

Z^2 is H, C1-4 alkyl, C1-4 alkoxy, nitro, halogen, trifluoromethyl, trifluoromethoxy, hydroxy or COR^1 (wherein R^1 is as hereinbefore defined.),
Z^3 is single bond or C1-4 alkylene,
Z^4 is SO_2 or CO,
Z^5 is

(1) C1-8 alkyl, C2-8 alkenyl, or C2-8 alkynyl,
(2) phenyl, C3-7 cycloalkyl, or 5-7 membered heterocyclic ring containing one or two oxygen, sulfur or nitrogen atom(s), or
(3) C1-4 alkyl, C2-4 alkenyl or C2-4 alkynyl substituted by phenyl or C3-7 cycloalkyl

(phenyl, C3-7 cycloalkyl, and 5-7 membered heterocyclic ring containing one or two oxygen, sulfur or nitrogen atom(s) mentioned in the above (2) and (3) may be substituted by 1-5 of R^5 (wherein R^5 (if two or more R^5, each independently) is H, C1-6 alkyl, C1-6 alkoxy, C1-6 alkylthio, nitro, halogen, trifluoromethyl, trifluoromethoxy or hydroxy).),
R^2 is

$CONR^8$,
NR^8CO,
$CONR^8$-C1-4 alkylene,
C1-4 alkylene-$CONR^8$,
NR^8CO-C1-4 alkylene,
C1-4 alkylene-NR^8CO,
C1-3 alkylene-$CONR^8$-C1-3 alkylene, or
C1-3 alkylene-NR^5CO-C1-3 alkylene
(wherein each R^8 is H or C1-4 alkyl.),
O, S, NZ^6
(wherein Z^6 is H or C1-4 alkyl.),

Z^7-C1-4 alkylene,
C1-4 alkylene-Z^7, or
C1-3 alkylene-Z^7-C1-3 alkylene
(wherein each Z^7 is O, S or NZ^6 (wherein Z^6 is as hereinbefore defined.).),
CO,
CO-C1-4 alkylene,
C1-4 alkylene-CO,
C1-3 alkylene-CO-C1-3 alkylene,
C2-4 alkylene,
C2-4 alkenylene, or
C2-4 alkynylene,

R^3 is H, C1-6 alkyl, C1-6 alkoxy, C1-6 alkylthio, nitro, halogen, trifluoromethyl, trifluoromethoxy, hydroxy or hydroxymethyl,
R^4 is

(1) H,
(2) C1-8 alkyl, C2-8 alkenyl, or C2-8 alkynyl,
(3) C1-6 alkyl substituted by one or two substituent(s) setected from the group consisting of $COOZ^8$, $CONZ^9Z^{10}$, and OZ^8, (wherein Z^8, Z^9 and Z^{10} each, independently, is H or C1-4 alkyl.) and C1-4 alkoxy-C1-4 alkoxy,
(4) C3-7 cycloalkyl, or
(5) C1-4 elkyl, C2-4 alkenyl or C2-4 elkynyl substituted by phenyl or C3-7 cycloalkyl

(phenyl and C3-7 cycloalkyl mentioned in the above (4) and (5) may be substituted by 1-5 of R^5 (wherein R^5 is as hereinbefore defined.).), and n end t eech, independently, is an integer of 1-4,
with the proviso that (1) R^2 and Z^3 should be connected at the 1- or 2- position of

. end (2) when

is a benzene ring end (Z^2)t is other than COR^1, Z^1 should be connected at the 3- or 4-position of the benzene ring.), or a non-toxic salt thereof,
(2) processes for preparing them and
(3) PGE_2 entegonists or egonists which comprise them as en ective ingredient.

Detailed Description of the Invention

[0021] In the formule (I), C1-4 etkyl in Z^5 end R^4 end C1-4 elkyl represented by Z^2, Z^6, Z^8, Z^9, Z^{10}, R^6, R^7 end R^8 means methyl, ethyl, propyl, butyl and isomer thereof.
[0022] In the formula (I), C1-6 alkyl in R^4 and C1-6 alkyl represented by R^3 and R^5 means methyl, ethyl, propyl, butyl, pentyl, hexyl end isomer thereot.
[0023] In the formula (I), C1-8 alkyl represented by Z^5 and R^4 means methyl, ethyl, propyl, butyl, pentyl, hexyl, heptyl, octyl and isomer thereof.
[0024] In the formula (I), C2-4 alkenyl in Z^5 and R^4 means vinyl, propenyl, butenyl and isomer thereot.
[0025] In the formule (I), C2-8 alkenyl represented by Z^5 and R^4 means C2-8 elkyl heving 1-3 of double bond and, for example, vinyl, propenyl, butenyl, pentenyl, hexenyl, heptenyl, octenyl etc. and isomer thereof.
[0026] In the formula (I), C2-4 alkynyl in Z^5 and R^4 means ethynyl, propynyl, butynyl and isomer thereof.
[0027] In the formula (I), C2-8 alkynyl represented by Z^5 and R^4 means C2-8 alkyl having 1-3 of triple bond and, for

example, ethynyl, propynyl, butynyl, pentynyl, hexynyl, heptynyl, octynyl etc. and isomer ther of.

[0028] In the formula (I), C1-4 alkoxy in R^4 and C1-4 alkoxy repres nted by Z^2 and R^1 means methoxy, ethoxy, propoxy, butoxy and isomer thereof.

[0029] In the formula (I), C1-6 alkoxy represented by R^3 and R^5 means methoxy, ethoxy, propoxy, butoxy, pentyloxy, hexyloxy and isomer thereof.

[0030] In the formula (I), C1-6 alkylthio represented by R^3 and R^5 means methylthio, ethylthio, propylthio, butylthio, pentylthio, hexylthio and isomer thereof.

[0031] In the formula (I), C1-3 alkylene in Z^1 end R^2 means methylene, ethylene, trimethylene and isomer thereof.

[0032] In the formula (I), C1-4 alkylene in Z^1 end R^2 and C1-4 alkylene represented by Z^3 means methylene, ethylene, trimethylene, tetramethylene and isomer thereof.

[0033] In the formula (I), C1-5 alkylene in Z^1 means methylene, ethylene, trimethylene, tetramethylene, pentamethylene and isomer thereof.

[0034] In the formula (I), C2-4 alkylene represented by R^2 means ethylene, trimethylene, tetramethylene and isomer thereof.

[0035] In the formula (I), C2-4 alkenylene represented by R^2 means vinylene, propenylene, butenylene and isomer thereof.

[0036] In the formula (I), C2-4 alkynylene represented by R^2 means ethynylene, propynylene, butynylene and isomer thereof.

[0037] In the formula (I), C3-7 cycloalkyl in Z^5 end R^4 and C3-7 cycloalkyl represented by Z^5 end R^4 means cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, cycloheptyl.

[0038] In the formula (I), C5-15 carbocyclic ring represented by

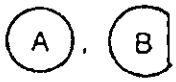
and

means mono-, bi- or tri-ring of C5-15 carbocyclic aryl, or partially or fully saturated ring thereof.

[0039] For example, C5-15 carbocyclic aryl includes benzene, pentalene, indene, naphthalene, azulene, fluorene, anthracene etc. Partially or fully saturated ring thereof includes the above mentioned ring which is partially or fully saturated.

[0040] As for C5-15 carbocyclic ring, preferably, mono- or bi-ring of C5-10 carbocyclic aryl and the mentioned C5-7 cycloalkyl is listed, and more preferebly, benzene, naphthalene, cyclopentyl, cyclohexyl or cycloheptyl.

[0041] In the formula (I), 5-7 membered heterocyclic ring containing one or two oxygen, sulfur or nitrogen atom(s) represented by



and Z^5 means 5-7 membered heterocyclic aryl ring containing one or two oxygen, sulfur or nitrogen atom(s) or partially or fully saturated ring thereof.

[0042] 5-7 membered heterocyclic aryl ring containing one or two oxygen, sulfur or nitrogen atom(s) includes pyrrole, imidazole, pyrazole, pyridine, pyrazine, pyrimidine, pyridazine, azepine, diazepine, furan, pyran, oxepine, oxazepine, thiophen, thiain (thiopyran), thiepine, oxazole, isoxazole, thiazole, isothiazole, oxadiazole, oxadiazine, oxazepine, oxadiazepine, thiediezole, thiediezine, thiediazepine etc.

[0043] 5-7 membered heterocyclic aryl ring containing one or two oxygen, sulfur or nitrogen atom(s) which is partially or fully saturated includes pyrroline, pyrrolidine, imidazoline, imidazolidine, pyrazoline, pyrazolidine, piperidine, piperazine, tetrahydropyrimidine, tetrahydropyridazine, dihydrofuran, tetrahydrofuran, dihydropyran, tetrahydropyran, dihydro-

thiophen, tetrahydrothiophen, dihydrothiain (dihydrothiopyran), tetrahydrothiain (tetrahydrothiopyran) , dihydroxazole, tetrahydroxazole, dihydroisoxazole, tetrahydroisoxazole, dihydrothiazole, tetrahydrothiazol , dihydroisothiazole, tetrahydroisothiazole, morpholine, thiomorpholine etc.

[0044] In the formula (I), halogen represented by Z^2, R^3 and R^5 means chlorine, bromine, fluorine and iodine.

[0045] In the formula (I), as for Z^3 which represents single bond or C1-4 alkylene, preferably, single bond or methylene is listed and more preferably, single bond.

[0046] In the formula (I), as for Z^4 which represents SO_2 or CO, preferably SO_2 is listed.

[0047] In the formula (I), as for R^4, preferebly, every group is listed and more preferably, group other then hydrogen

[0048] Unless otherwise specified, all isomers are included in the invention. For example, alkyl, alkylene and alkenylene includes straight-chain or branched-chain ones. Double bond in alkenylene include structure of configurations E, Z and EZ mixtures. Isomers generated by asymmetric carbon(s) e.g. branched alkyl are also included in the present invention.

[0049] In the compounds of the formula (I) of the present invention, the compounds wherein

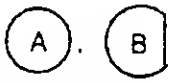
and

is C5-15 carbocyclic ring and Z^5 is C1-8 alkyl, C2-8 alkenyl, C2-8 alkynyl, or group containing phenyl or C3-7 cycloalkyl (each ring may be substituted.) are preferable. The compounds wherein

and

is mono- or bi-ring of C5-10 carbocyclic eryl end C5-7 cycloalkyl end Z^5 is the above mentioned group are more preferable.

[0050] The compounds wherein at least one of



and Z^5 is 5-7 membered heterocyclic ring containing one or two oxygen, sulfur or nitrogen atom(s) (each ring may be substituted.) are also preferable. Such compounds include, for exemple, the compounds wherein (1)

and

is C5-15 carbocyclic ring and Z^5 is 5-7 membered heterocyclic ring containing one or two oxygen, sulfur or nitrogen atom(s) or (2) one of

and

is 5-7 membered heterocyclic ring containing one or two oxygen, sulfur or nitrogen atom(s) and the other is C5-15 carbocyclic ring. The compounds wherein carbocyclic ring represented by

and/or

in case of the above (1) and (2) is mono- or bi-ring of C5-10 carbocyclic aryl and C5-7 cycloalkyl are more preferable.

[0051] In the compounds of the formula (I) of the present invention, concrete and preferable compounds include the compounds described in the Examples and corresponding esters and amides.

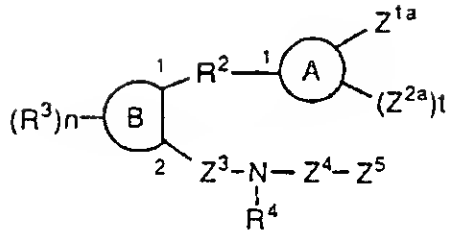
[Salt]

[0052] The compounds of the present invention of the formula (I) maybe converted into the corresponding salts by methods known per se. Non-toxic and water-soluble salts are preferable. Suitable salts, for example, are as follows: salts of alkali metals (potassium, sodium etc.), salts of alkaline earth metals (calcium, magnesium etc.), ammonium salts, salts of pharmaceutically acceptable organic amines (tetramethylammonium, triethylamine, methylamine, dimethylamine, cyclopentylamine, benzylamine, phenethylamine, piperidine, monoethanolamine, diethanolamine, tris(hydroxymethyl)aminomethene, lysine, arginine, N-methyl-D-glucamine etc.).

[The method of the preparation for the present invention compounds]

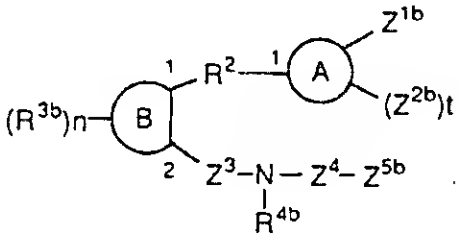
[0053] The compounds of the formula (I) of the present invention may be prepared by the method described in the following, the method described in the Examples as hereinafter or known methods.

(1) In the compounds of the formula (I) of the present invention, the carboxylic acid compounds of the formula (Ia)



(Ia)

(wherein Z^{1a} and Z^{2a} ere as Z^1 and Z^2, respectively, with the proviso that at least one of them is COOH or a group containing COOH, and the other symbols are as hereinbefore defined.)
may be prepared from the ester compound of the formula (Ib)

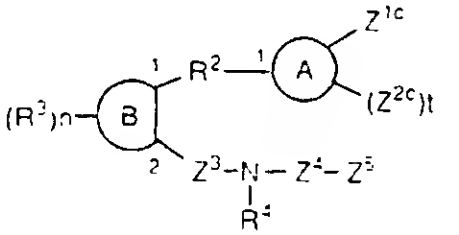


(Ib)

(wherein Z^{1b} and Z^{2b} are as Z^1 and Z^2, respectively, with the proviso that at least one of them is COR^{1b} or a group containing COR^{1b} (wherein R^{1b} is C1-4 alkoxy or methoxymethoxy (abbreviated as OMOM.).), R^{3b}, R^{4b} and Z^{5b} are as R^3, R^4 and Z^5, respectively, with the proviso when R^3, R^4 or R^5 in Z^5 is COOH or hydroxy, or e group containing COOH or hydroxy, each COOH and hydroxy is protected by a protecting group which is removable under an acidic, neutral or alkaline condition, and the other symbols are as hereinbefore defined.)
by hydrolysis under an alkaline, acidic or neutral condition, if necessary, followed by hydrolysis under the different condition.

The removal of a protecting group by hydrolysis under an alkaline, acidic or neutral condition is a well-known reaction as hereinafter described.

(2) In the compounds of the formula (I) of the present invention, the ester compounds of the formula (Ic)



(Ic)

(wherein Z^{1c} and Z^{2c} ere as Z^1 and Z^2, respectively, with the proviso that at least one of them is COR^{1c} or a group containing COR^{1c} (wherein R^{1c} is C1-4 alkoxy.) end the other symbols are as hereinbefore defined.) may be prepared from the compound of the formula (Ia) by esterification.

Esterification is well known, it may be carried out, for example;

(a) by the method using diazoalkane,
(b) by the method using alkyl halide,
(c) by the method using dimethylformamide (DMF)-dialkyl acetal or

(d) by the method reacting corresponding alkanol etc.

Concrete description of the methods described above are as follows.

(a) The method using diazoalkane may be carried out, for example, using corresponding diezoalkane in an organic solvent (diethylether, ethyl acetate, methylene chloride, acetone, methanol or ethanol etc.) at -10~40°C.

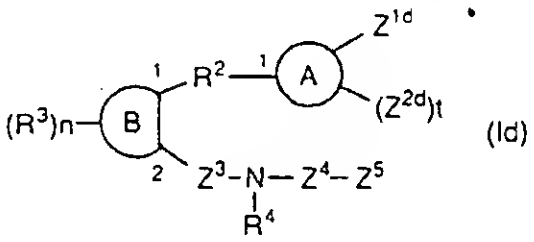
(b) The method using alkyl halide may be carried out, for example, in an organic solvent (acetone, DMF, dimethylsufoxide (DMSO) etc.) in the presence of base (potassium carbonate, sodium carbonate, potassium hydrogen carbonate, sodium hydrogen carbonate, calcium oxide etc.) using corresponding alkyl halide at -10~40°C.

(c) The method using DMF-dialkyl acetal may be carried out, for example, in an organic solvent (benzene, toluene etc.) using corresponding DMF-dialkyl acetal at -10~40°C.

(d) The method of reacting corresponding alkanol may be carried out, for example, in corresponding alkanol (HR^{1c} (R^{1c} is as hereinbefore defined.)) using acid (HCl, sulfuric acid, p-toluene sulfonic acid, hydrochloride gas etc.) or condensing egents (DCC, pivaloyl halide, aryl sulfonyl halide, alkyl sulfonyl halide etc.) at 0~40°C.

Of course, an organic solvent (tetrahydrofuran, methylene chloride etc.) which does not relate to the reaction mey be edded in these esterification.

(3) In the compounds of the formula (I) of the present invention, the amide compounds of the formula (Id)



(Id)

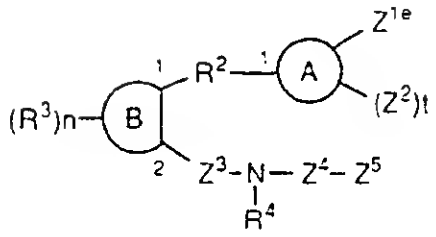
(wherein Z^{1d} and Z^{2d} are as Z^1 and Z^2, respectively, with the proviso that at least one of them is COR^{1d} or a group containing COR^{1d} (wherein R^{1d} is NR^6R^7 (wherein all symbols are as hereinbefore defined.), and the other symbols are as hereinbefore defined.) may be prepered by reacting the compound of the formula (Ia) with the compound of the formula (III)

$$HNR^6R^7 \qquad \text{(III)}$$

(wherein all symbols are as hereinbefore defined.) to form the amide bond.

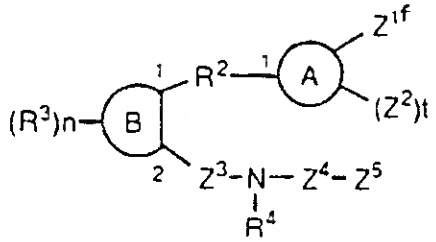
Reaction to form amide-bond is well known, it may be carried out, for example, in an organic solvent (THF, methylene chloride, benzene, acetone, acetonitrile etc.), in the presence or absence of tertiary amine (dimethylaminopyridine, pyridine, triethylamine etc.) using a condensing agent (EDC or DCC etc.) et 0~50°C.

(4) In the compounds of the formula (I) of the present invention, the alcohol compounds of the formula (Ie)



(Ie)

(wherein Z^{1e} is C1-5 alkylene-OH, and the other symbols are as hereinbefore defined.) may be prepared by the reduction of the compound of the formula (If)

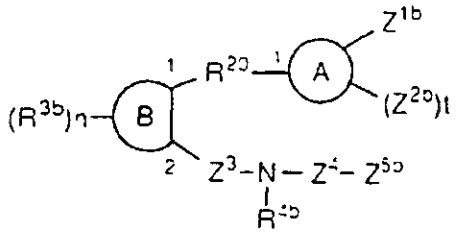


(If)

(wherein Z^{1f} is $COOY^f$ or C1-4 alkylene-$COOY^f$ (wherein Y^f is C1-4 alkyl.), and the other symbols are as hereinbefore defined.).

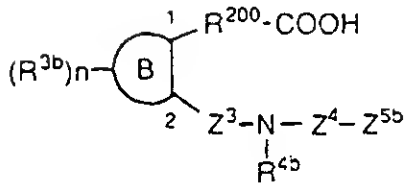
The reductive reaction is known, and for exemple, this reaction may be carried out in the presence of organic solvent (THF, methylene chloride, diethylether, lower alkanol etc.) using lithium aluminum hydride (LAH) or diisobutyl aluminum hydride (DIBAL) at -78°C to room temperature.

(5) In the compounds of the formula (Ib), wherein R^2 is $CONR^8$, C1-4 alkylene-$CONR^8$, $CONR^8$-C1-4 alkylene, C1-3 alkylene-$CONR^8$-C1-3 alkylene, (wherein all symbols are as hereinbefore defined.), i.e. the compounds of the formula (Ib-1)



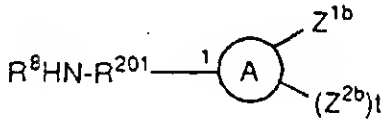
(Ib-1)

(wherein R^{2b} is $CONR^8$, C1-4 alkylene-$CONR^8$, $CONR^8$-C1-4 alkylene, C1-3 alkylene-$CONR^8$-C1-3 alkylene, (wherein all symbols are as hereinbefore defined.), and the other symbols are as hereinbefore defined.) may be prepared by reacting the compound of the formula (IV)



(IV)

(wherein R^{200} is single bond or C1-4 alkylene, and the other symbols are as hereinbefore defined.) with the compound of the formula (V)

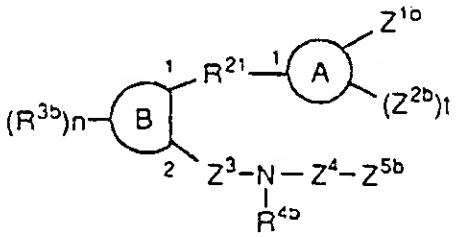


(V)

(wherein R^{201} is single bond or C1-4 alkylene, and the other symbols are as hereinbefore defined.) to form amide bond.

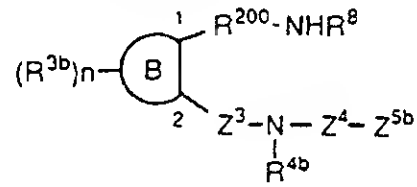
Reaction to form amide bond may be carried out as the method described in the said (3).

(6) In the compounds of the formula (Ib), wherein R^2 is NR^8CO, C1-4 alkylene-NR^8CO, NR^8CO-C1-4 alkylene, C1-3 alkylene-NR^8CO-C1-3 alkylene (wherein all symbols are as hereinbefore defined.), i.e. the compounds of the formula (Ib-2)



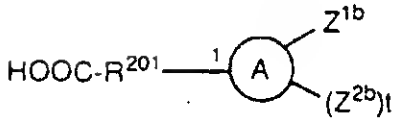
(Ib-2)

(wherein R^{21} is NR^8CO, C1-4 alkylene-NR^8CO, NR^8CO-C1-4 alkylene, C1-3 alkylene-NR^8CO-C1-3 alkylene (wherein all symbols are as hereinbefore defined.), and the other symbols are as hereinbefore defined.) may be prepared by reacting the compound of the formula (VI)



(VI)

(wherein all symbols are as hereinbefore defined.) with the compound of the formula (VII)

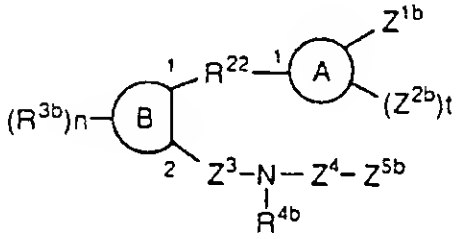


(VII)

(wherein all symbols are as hereinbefore defined.)
to form amide bond.

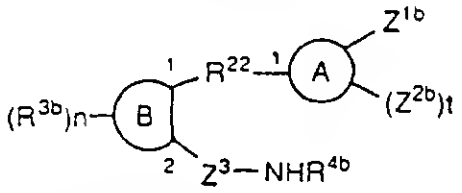
Reaction to form amide bond may be carried out as the method described in the said (3).

(7) In the compounds of the formula (Ib), wherein R^2 is O, S, NZ^6, Z^7-C1-4 alkylene, C1-4 alkylene-NZ^7 or C1-3 alkylene-NZ^7-C1-3 alkylene (wherein all symbols are as hereinbefore defined.), i.e. the compounds of the formula (Ib-3)



(Ib-3)

(wherein R^{22} is O, S, NZ^6, Z^7-C1-4 alkylene, C1-4 alkylene-NZ^7 or C1-3 alkylene-NZ^7-C1-3 alkylene (wherein all symbols are as hereinbefore defined.).)
may be prepared by reacting the compound of the formula (VIII)



(VIII)

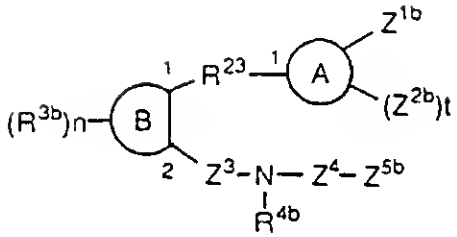
(wherein all symbols are as hereinbefore defined.)
with the compound of the formula (IX)

$$X\text{-}Z^4\text{-}Z^{5b} \qquad \text{(IX)}$$

(wherein X is halogen and the other symbols are as hereinbefore defined.) to form sulfonamide bond or carboamide bond.

Reactions to form sulfonamide bond or carbcamide bond may be carried out, for example, in an organic solvent (THF, methylene chloride, benzene, acetone, acetonitrile etc.), in the presence or absence of tertiary amine (dimethylaminopyridine, pyridine, triethylamine etc) at 0~50°C.

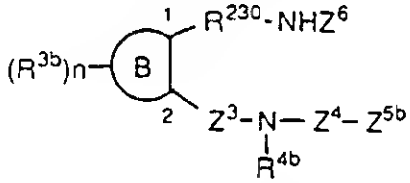
(8) In the compounds of the formula (Ib), wherein R^2 is NZ^6-C1-4 alkylene, C1-4 alkylene-NZ^6 or C1-3 alkylene-NZ^6-C1-3 alkylene (wherein all symbols are as hereinbefore defined.), i.e. the compounds of the formula (Ib-4)



(Ib-4)

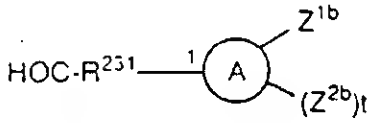
(wherein R^{23} is NZ^6-C1-4 alkylene, C1-4 alkylene-NZ^6 or C1-3 alkylene-NZ^6-C1-3 alkylene (wherein all symbols are as hereinbefore defined.) and the other symbols are as hereinbefore defined.)
may be prepared by

(a) reacting (reductive amination) the compound of the formula (VI-a)



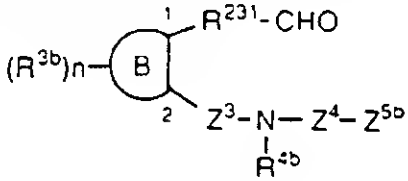
(VI-a)

(wherein R^{230} is single bond or C1-4 alkylene, and the other symbols are as hereinbefore defined.)
with the compound of the formula (VII-a)



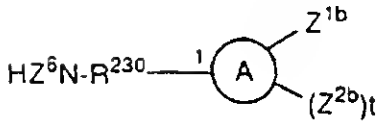
(VII-a)

(wherein R^{231} is single bond or C1-3 alkylene, and the other symbols are as hereinbefore defined.) or
(b) reacting (reductive amination) the compound of the formula (VI-b)



(VI-b)

(wherein all symbols are as hereinbefore defined)
with the compound of the formula (VII-b)

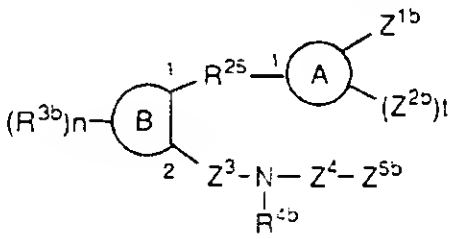


(VII-b)

(wherein all symbols are as hereinbefore defined.).

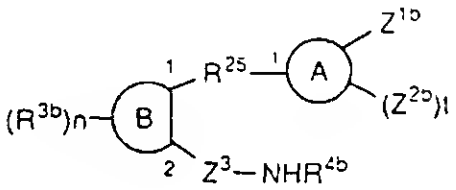
The reaction of reductive amination described in tha above (a) and (b) may carried out, for example, in organic solvent (methanol atc.), in an acidic condition, using a boron reagent such as sodium cyanoborohydride etc. at 0~50°C.

(9) In the compounds of the formula (Ib), wherein R^2 is C2-4 alkenylene, i.e. the compounds of the formula (Ib-5)



(Ib-5)

(wherein R^{25} is C2-4 alkenylene and the other symbols are as hereinbefore defined.)
may be prepared by reacting the compound of the formula (XI)



(XI)

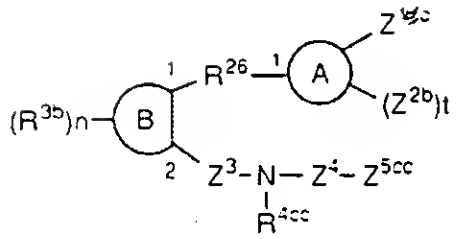
(wherein all symbols are as hereinbefore defined)
with the compound of the formula (IX)

$$X\text{-}Z^4\text{-}Z^{5b} \qquad \text{(IX)}$$

(wherein all symbols are as hareinbefore defined.)
to form sulfonamide bond or carboamide bond.

Reaction to form sulfonamide bond or carboamide bond may be carried out as the method described in the said (7).

(10) In the compounds of the formula (Ib), wherein R^2 is C2-4 alkylene, i.e. the compounds of tha formula (Ib-6)

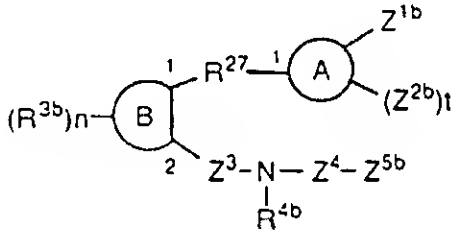


(Ib-6)

(wherein R^{26} is C2-4 alkylene, Z^{1cc}, Z^{5cc} and Z^{4cc} are as Z^{1b}, Z^{5b} and Z^{4b}, respectively, with the proviso that none of Z^{1cc}, Z^{5cc} and Z^{4cc} are alkylenylene, alkynylene, alkenylene-containing group and alkynylene-containing group, and the other symbols are as hereinbefore defined.)
may be prepared by catalytic reduction of the compound of the formula (Ib-5).

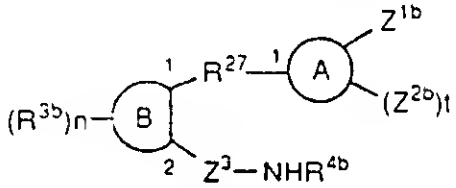
The catalytic reduction is known, and for example, this reaction may be carried out under the condition of atmosphere of hydrogen gas, in an organic solvent (THF, alkanol or acetone etc.), using a reductive catalyst (Pd, Pd-C, Pt or platinum oxide etc.) at 0~50°C.

(11) In the compounds of the formula (Ib), wherein R^2 is C2-4 alkynylene, i.e. the compounds of the formula (Ib-7)



(Ib-7)

(wherein R^{27} is C2-4 alkynylene, and the other symbols are as hereinbefore defined.)
may be prepared by reacting the compound of the formula (XII)



(XII)

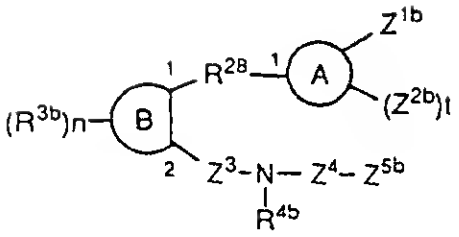
(wherein all symbols are as hereinbefore defined.)
with the compound of the formula (IX)

$$X\text{-}Z^{4}\text{-}Z^{5b} \qquad \text{(IX)}$$

(wherein all symbols are as hereinbefore defined.)
to form sulfonamide bond or carboamide bond.

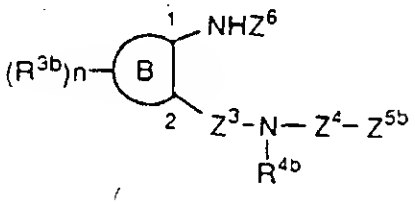
Reaction to form sulfonamide bond or carboamide bond may be carried out as the method described in the said (7)

(12) In the compounds of the formula (Ib), wherein R^2 is NZ^6SO_2 (wherein all symbols are as hereinbefore defined.), i.e. the compounds of the formula (Ib-8)



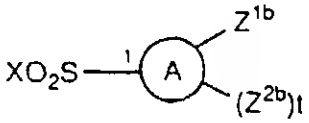
(Ib-8)

(wherein R^{28} is NZ^6SO_2 (wherein e' symbols ere es hereinbefore defined.), end the other symbols are es hereinbefore defined.)
may be prepared by reacting the compound of the formula (Z-1)



(Z-1)

(wherein all symbols are as hereinbefore defined.)
with the compound of the formula (Z-2)

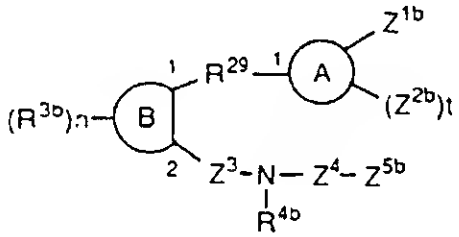


(Z-2)

(wherein all symbols are as hereinbefore defined.)
to form sulfonamide bond.

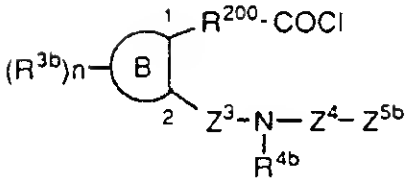
Reaction to form sulfonamide bond may be carried out as the method described in the said (7).

(13) In the compounds of the formula (Ib), wherein R^2 is CO, CO-C1-4 alkylene, C1-4 alkylene-CO or C1-3 alkylene-CO-C1-3 alkylene, i.e. the compounds of the formula (Ib-9)



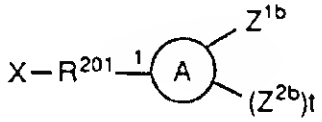
(Ib-9)

(wherein R^{29} is CO, CO-C1-4 alkylene, C1-4 alkylene-CO or C1-3 alkylene-CO-C1-3 alkylene, and the other symbols ere es hereinbefore defined.) may be prepared by reecting the compound of the formula (Z-3)



(Z-3)

(wherein all symbols are as hereinbefore defined.)
with the compound of the formula (Z-4)

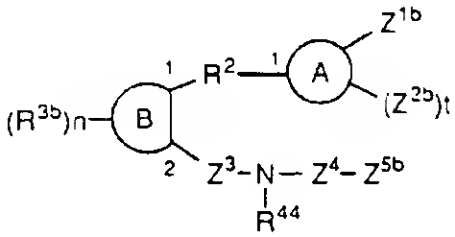


(Z-4)

(wherein all symbols are as hereinbefore defined.)

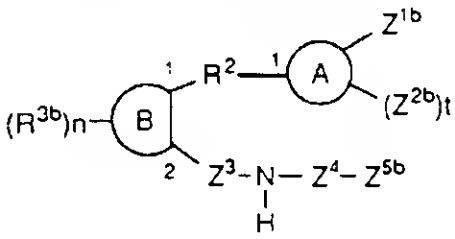
This reaction may be carried out, for example, in organic solvent (THF, methylene chloride, benzene, acetone, acetonitrile etc.) in the presence of Zn or cyano copper at -78°C to room temperature.

(14) In the compounds of the formula (Ib), wherein R^{4b} is group other than H, i.e. the compounds of the formula (Ib-10)



(Ib-10)

(wherein R^{44} is as R^4 other than H, and the other symbols are as hereinbefore defined.)
may be prepared by reacting the compound of the formula (Ib-11)



(Ib-11)

(wherein all symbols are as hereinbefore defined.)
and (e) the compound of the formula (Z-5)

(Z-5)

(wherein all symbols are as hereinbefore defined.)
or (b) the compound of the formule (Z-6)

$$HO—R^{44} \quad (Z\text{-}6)$$

(wherein all symbols are as hereinbefore defined.).

The above reaction is N-alkylation reaction or corresponding reaction. For example, this reaction (a) in case of using alkyl helide of the formule

$$X\text{-}R^{44}$$

(wherein all symbols are as hereinbefore defined.),
may be carried out in organic solvent (acetone, THF or methylene chloride etc.), in the presence of base (potassium carbonate etc.) at 0~50°C.

The reaction (b) in case of using alcohol of the formule

$$HO\text{-}R^{44}$$

(wherein all symbols are as hereinbefore defined.),
may be carried out in organic solvent (acetone, THF or methylene chloride etc.), in the presence of triphenylphosphine and diethyldiazocarboxylate (DEAD) at 0~50°C.

(15) The compounds wherein R^3 is hydroxymethyl may be prepared by the method mentioned above or the method described in the Examples hereinafter.

(16) The compounds wherein Z^4 is SO_2 and Z^5 is cyclopentyl, cyclohexyl (each ring may be substituted by 1-5 of R^5 (R^5 is as hereinbefore defined.).) or isopropyl may be prepared by the method mentioned above or the method described in the Examples hereinafter.

(17) The compounds wherein symbol(s) other than Z^1 is/are COOH, $COOZ^a$ (wherein Z^a is C1-4 alkyl) or hydroxy or group containing COOH, $COOZ^a$ (wherein Z^a is as hereinbefore defined.) or hydroxy
may be prepered by reacting under the condition thet each of the above groups end Z^1 if necessay are protected by a protecting group which is removable under en elkaline, ecidic or neutral condition and removing a protecting group under an alkaline, acidic or neutral condition or combining removal of protecting groups under different conditions (for example, removal of a protecting group under an acidic condition and removal of a protecting group under en alkaline condition mey be cerried out successively, either reection being started tirst.).

[0054] A protecting group of COOH which is removable under an acidic condition includes, for example, silyl containing group such as t-butyldimethylsilyl etc. or t-butyl.

[0055] A protecting group of COOH which is removeble under en alkaline condition includes alkyl group (for example, methyl etc.) other than t-butyl.

[0056] A protecting group of COOH which is removable under both an acidic condition and an alkaline condition includes, for exemple, methoxymethyl.

[0057] A protecting group of COOH which is removable under a neutral condition includes benzyl etc.

[0058] A protecting group of hydroxy which is removable under an acidic condition includes, for example, tetrahydropyranyl, silyl containing group such as t-butyldimethylsilyl etc. 1-ethoxyethyl or methoxymethyl etc.

[0059] A protecting group of hydroxy which is removable under en alkaline condition includes ecyl group such es acetyl etc.

[0060] A protecting group of hydroxy which is removable under a neutral condition includes benzyl or silyl containing group such as t-butyldimethylsilyl etc.

[0061] The removal of e protecting group under an elkaline condition is well known. For example, this reection may be carried out in an organic solvent (methanol, THF, dioxane etc.), using a hydroxide of an alkali metal (sodium hydroxide, potassium hydroxide etc.), a hydroxide of an alkaline earth metal (calcium hydroxide etc.) or a carbonate salt (sodium carbonete, potessium carbonete etc.) or en equeous solution thereof, or mixture thereof et 0~40°C.

[0062] The removal of a protecting group under an acidic condition is well known. For example, this reaction may be carried out in a solvent (methylene chloride, dioxane, ethyl acetate, acetic acid, water or mixture thereof etc.), using an organic acid (trifluoroacetic acid etc.) or an inorganic acid (HCl, HBr etc.) at 0~120°C.

[0063] The removal of a protecting group under a neutral condition is well known. For example, this reaction using benzyl may be carried out in a solvent (ether (THF, dioxane, dimethoxyethane, diethyl ether etc.), alcohol (methanol, ethanol etc.), benzene (benzene, toluene etc.), ketone (acetone, methylethyl ketone etc.), nitrile (acetonitrile etc.) amide (dimethylformamide etc.) water, ethyl acetate, acetic acid or mixture thereof etc.) in the presence of catalyst (Pd-C, palladium black, PdOH, PtO_2, Raney nickel etc.), at ordinary or increased pressure under the condition of atmosphere of hydrogen gas or in the presence of ammonium formate at 0~200°C.

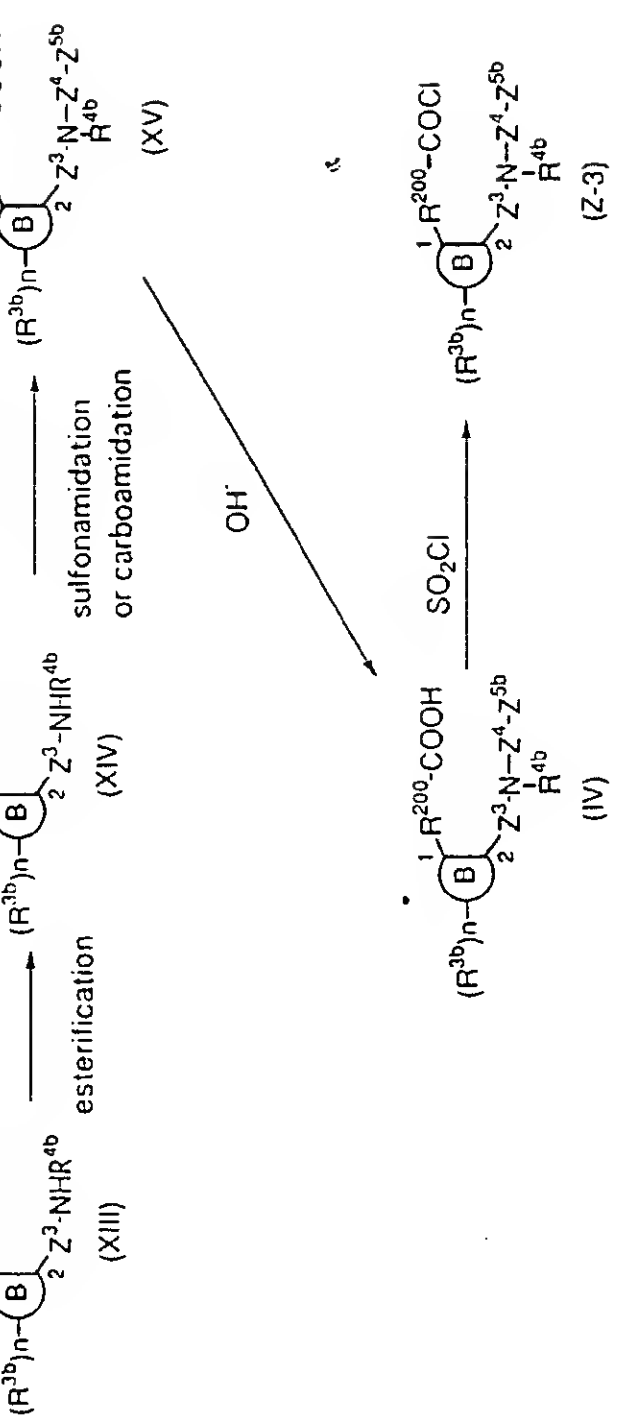
[0064] This reaction using silyl containing group such as t-butyldimethylsilyl etc. may be carried out in a solvent such as ether (THF etc.), using tetrabutylammonium fluoride at 0~50°C.

[0065] The compounds of the formula (III), (V), (VII), (IX), (VII-a), (VII-b), (Z-2), (Z-4), (Z-5) or (Z-6) are known or may be prepared easily by known methods or the methods described in the Examples hereinafter. The compounds of the formula (IV), (VI), (VIII), (X), (XI), (XII) or (Z-3) may be prepared by the following reaction schemes (A)-(F).

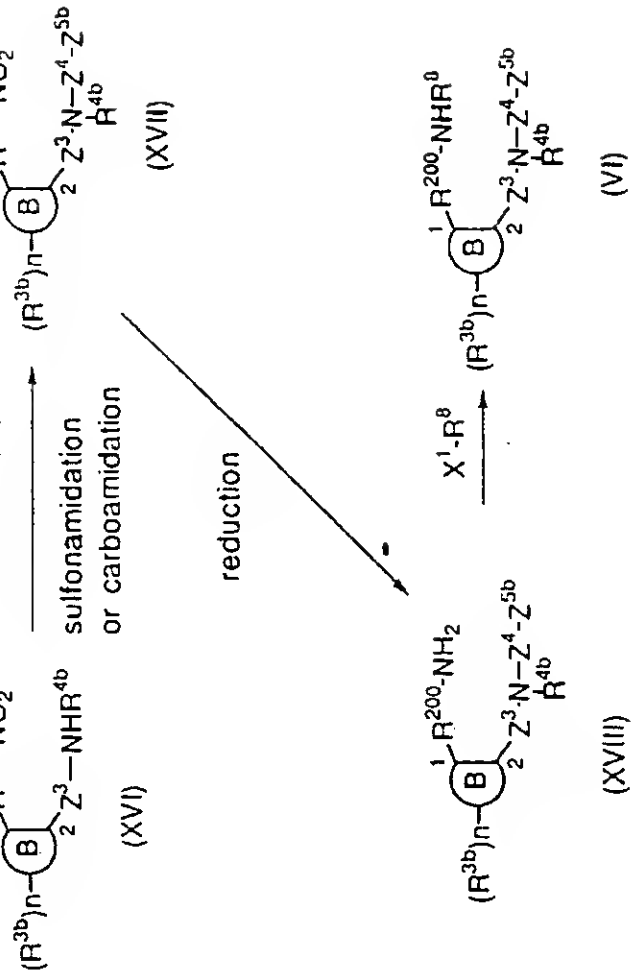
[0066] In each reaction scheme, each symbol is as hereinbefore defined, or as defined as follows.

R^{200} : single bond or C1-4 alkylene;
R^{202} : single bond or C1-4 alkylene;
R^{203} : single bond or C1-4 alkylene;
R^{204} : single bond or C1 or 2 alkylene;
R^{205} : C1, 2 or 3 alkylene;
R^{206} : single bond or C1 or 2 alkylene;
R^{207} : C1, 2 or 3 alkylene;
R^{208} : C1 or 2 alkylene;
R^{50} : C1-4 alkyl;
R^{51} : trifluoroacetyl;
X^1, X^2, X^3, X^4 : halogen.

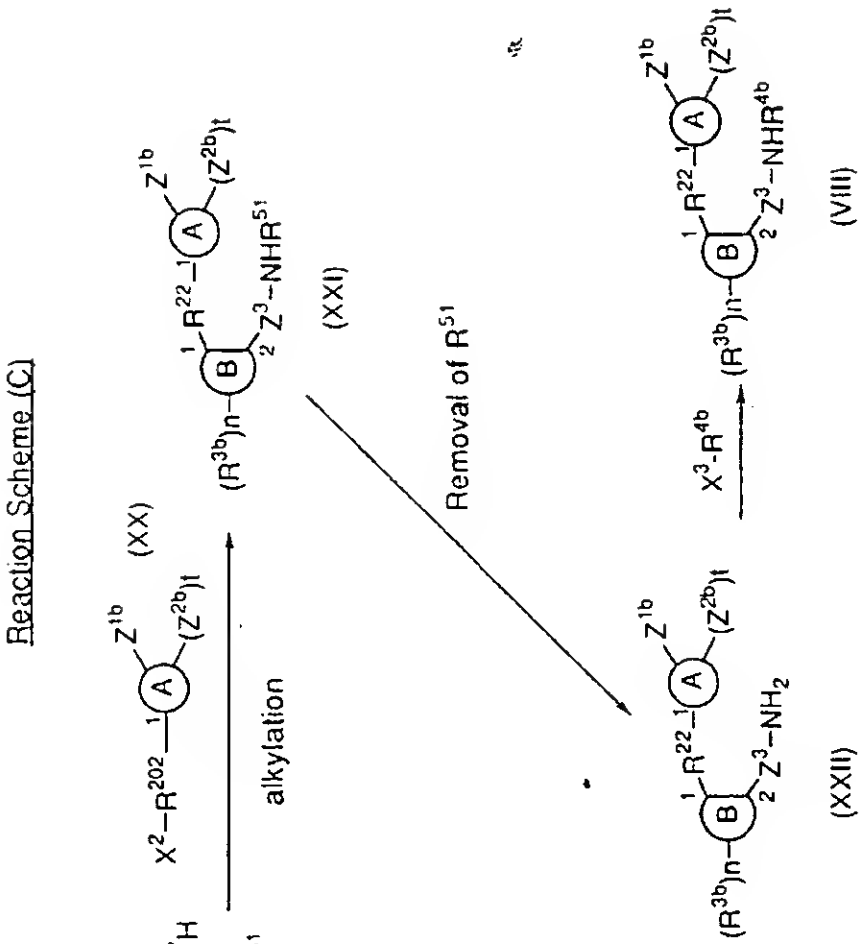
Reaction Scheme (A)



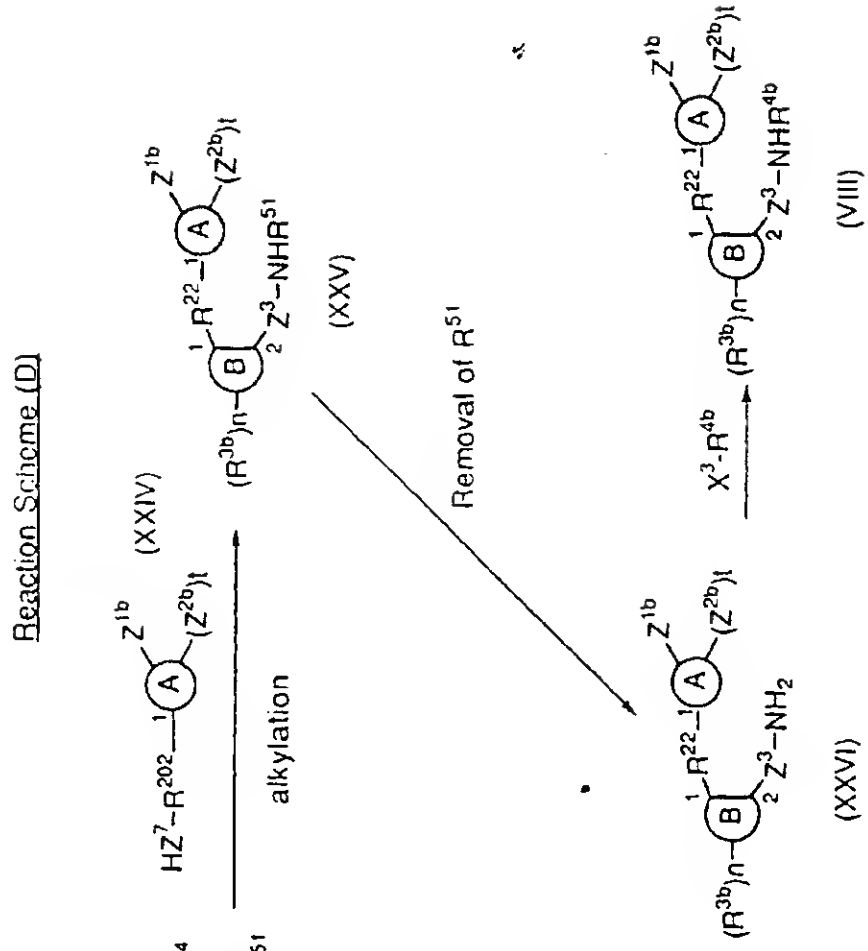
Reaction Scheme (B)



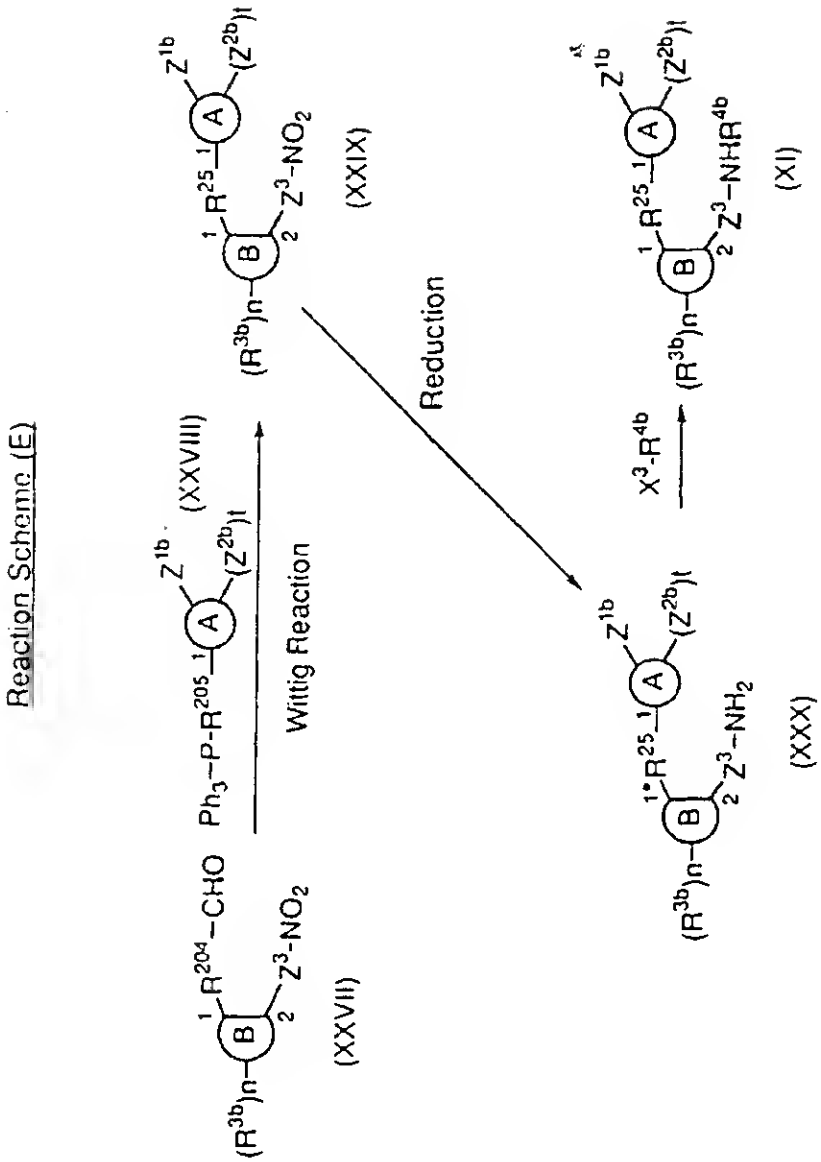
Reaction Scheme (C)



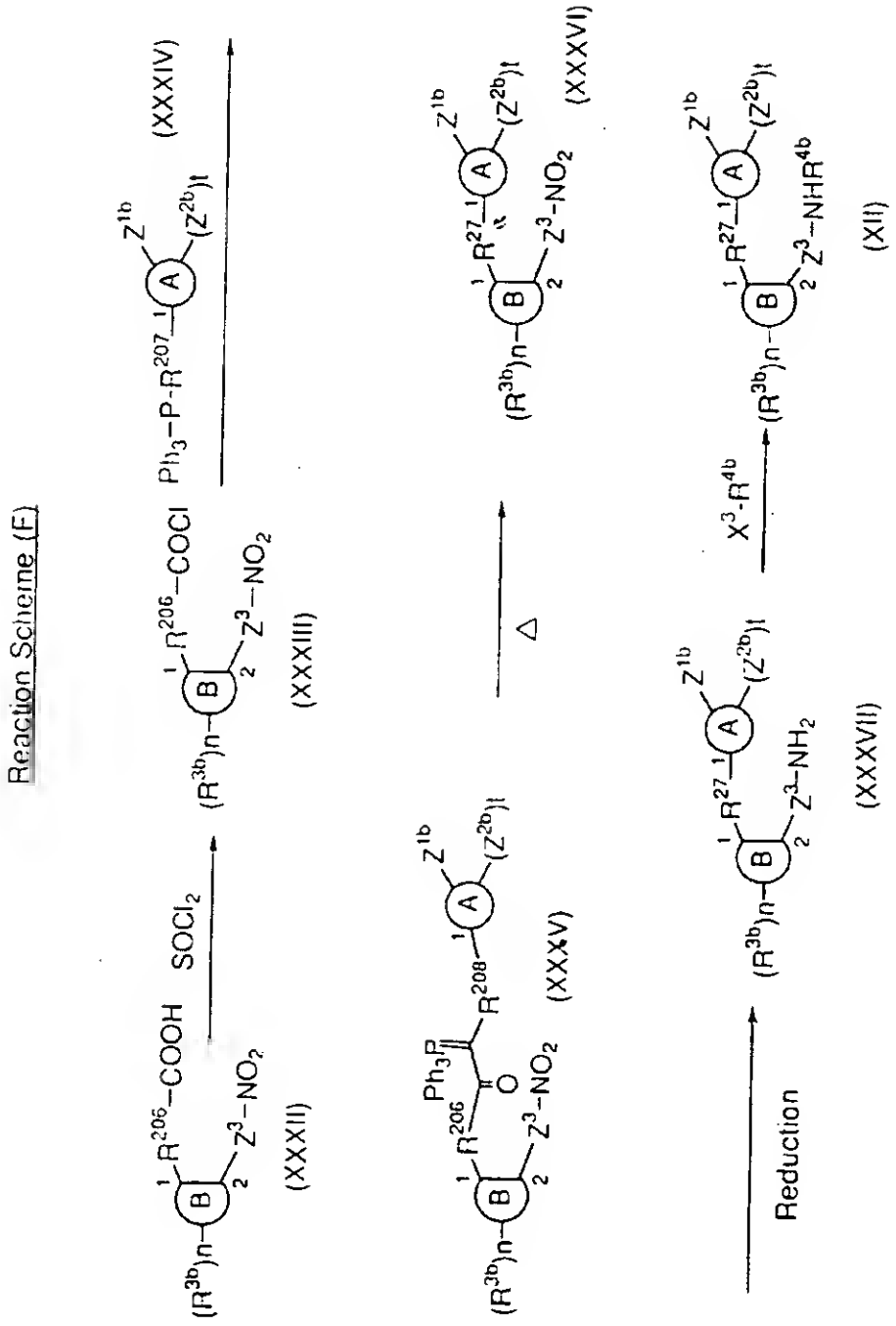
Reaction Scheme (D)



Reaction Scheme (E)



Reaction Scheme (F)



[0067] In each reaction in the present specification, obtained products may be purified by conventional techniques. For example, purification may be carried out by distillation at atmospheric or reduced pressure, by high performance liquid chromatography, by thin layer chromatography or by column chromatography using silica gel or magnesium silicate, by washing or by recrystallization. Purification may be carried out after each reaction, or after a series of reactions.

[Starting materials and reagents]

[0068] The other starting materials and reagents in the present invention are known per se or may be prepared by known methods.

Industrial Availability

[Pharmacological activity of the present invention compounds]

[0069] The compounds of the present invention of the formula (I) can bind to the receptors of prostaglandin E_2 and show antagonistic activity against the action thereof or agonistic activity, so they are useful as PGE_2 antagonists or agonists.

[0070] As mentioned hereinbefore, to antagonize against PGE_2 is linked to inhibition of uterine contraction, analgesic action, inhibition of digestive peristalsis, induction of sleep or increase of vesical capacity. Therefore, PGE_2 antagonists are considered to be useful for the prevention of abortion, as analgesics, as antidiarrheals, as sleep inducers or as agents for treating pollakiuria.

[0071] As mentioned hereinbefore, to show PGE_2 agonistic activity is linked to uterine contraction, promotion of digestive peristalsis, suppression of gastric acid secretion or reduction of blood pressure or diuresis. Therefore, PGE_2 agonists are considered to be useful as abortifacient, cathartic, antiulcer, anti-gastritis, antihypertensive or diuretic agents.

[0072] For example, in standard laboratory test, it was confirmed that the compounds of the formula (I) of the present invention can bind to receptor of PGE_2 (EP_1 receptor) according to assay using expression cell of prostanoid receptor subtype.

(i) Binding assay using expression cell of prostanoid receptor subtype

[0073] The preparation of membrane fraction was carried out according to the method of Sugimoto et al (J. Biol. Chem. 267, 6463-6466 (1992)), using expression CHO cell of prostanoid receptor subtype (mouse EP1).

[0074] The standard assay mixture contained membrane fraction (0.5 mg/ml), ^{3}H-PGE_2 in a final volume of 200 ml was incubated for 1 hour at room temperature. The reaction was terminated by addition of 3 ml of ice-cold buffer. The mixture was rapidly filtered through a glass filter (GF/B). The radioactivity associated with the filter was measured by liquid scintillation counting.

[0075] Kd and Bmax values were determined from Scatchard plots (Ann. N.Y. Acad. Sci, 51, 660 (1949)). Non-specific binding was calculated as the bond in the presence of an excess (2.5 nM) of unlabeled PGE_2. In the experiment for competition of specific ^{3}H-PGE_2 binding by the compounds of the present invention, ^{3}H-PGE_2 was added at a concentration of 2.5 nM and the compound of the present invention was added at a concentration of 1 μM. The following buffer was used in all reaction.

Buffer potassium phosphate (pH6.0, 10 mM), EDTA (1 mM), $MgCl_2$ (10 mM), NaCl (0.1 M).

The dissociation constant Ki (μM) of each compound was calculated by the following equation.

$$Ki = IC50/(1+([C]/Kd))$$

The results were shown in Table 1.

Table 1

Example No.	dissociation constant Ki (μM)
2 (k)	0.099
18 (30)	0.0016
18 (38)	0.016
18 (58)	0.0062
18 (75)	0.0054
18 (94)	0.0004
18 (102)	0.0002

Table 1 (continued)

Example No.	dissociation constant Ki (μM)
20 (20)	0.0099
22 (3)	0.48
24	0.0058
24 (9)	0.018
30	0.073
38	0.16
43	0.38
44	0.0013
48	0.01

[Toxicity]

[0076] The toxicity of the compounds of tha presant invantion is vary low and therefore, it is confirmed that thasa compounds are safe for use as medicine.

[Application for Pharmaceuticals]

[0077] The compounds of the present invention of the formula (I) can bind to the receptors of prostaglandin E_2 and show antagonistic activity against tha action thereof or agonistic activity, so they ara useful as PGE_2 antagonists or agonists.

[0078] As mentioned hereinbefore, to antagonize against PGE_2 is linked to inhibition of uterine contraction, analgesic action, inhibition of digestive peristalsis, induction of sleep or increase of vesical capacity. Therefore, PGE_2 antagonists are considered to be useful for the prevention of abortion. as analgesics, as antidiarrheals, as sleep inducers or as agents for treating pollakiuria.

[0079] As mentioned hereinbefore. to show PGE_2 agonistic activity is linked to uterine contraction, promotion of digestive peristalsis, suppression of gastric acid secretion or reduction of blood pressure or diuresis. Therefore, PGE_2 agonists are considered to be useful as abortifacient. cathartic, antiulcer, anti-gastritis, antihypertensive or diuretic agents.

[0080] The compounds of the present invention can bind to receptors of prostaglandin E_2, especially, EP1 receptor strongly, so they are expected to be useful as analgesics or as agents for traating pollakiuria.

[0081] For the purpose above described, the compounds of the formula (I), non-toxic salts thereof and hydrates thareof may be normally administered systamically or locally, usually by oral or parenteral administration.

[0082] The doses to be administered are determined depending upon age, body weight, symptom, the desired therapeutic effect. the route of administration, and the duration of the treatment etc. In the human adult, the doses per parson per dose are generally between 1 μg and 100 mg, by oral administration, up to several times per day, and between 0.1 μg and 10 mg, by parenteral administration (preferred into vein) up to several times par day, or continuous administration between 1 and 24 hours per day into vein.

[0083] As mentioned above, the doses to be used depend upon various conditions. Therefore, there are cases in which doses lowar than or greater than tha rangas specified above may ba used.

[0084] On administration of the compounds of the present invention, it is used as solid compositions, liquid compositions or other compositions for oral administration, as injections, liniments or suppositories etc. for parenteral administration.

[0085] Solid compositions for oral administration include comprassed tablats, pills, capsules, dispersible powders, and granules etc.

[0086] Capsules contain hard capsules and soft capsules.

[0087] In such solid compositions, one or more of the active compound(s) is or are, admixed with at least one inert diluent such as lactosa, mannitol, mannit, glucose, hydroxypropyl callulosa, microcrystallina cellulose, starch, polyvinylpyrrolidone, magnesium metasilicate aluminate. The compositions may also comprise, as is normal practice, additional substances other than inert diluents: e.g. lubricating agents such as magnesium stearate, disintegrating agents such as callulosa calcium glycolata, and assisting agents for dissolving such as glutamic acid or asparaginic acid. Tha tablets or pills may, if desired, be coated with film of gastric or enteric material such as sugar, gelatin, hydroxypropyl cel-

lulose or hydroxypropyl callulose phthalate etc., or be coated with two or more films. And further, coating may include containment within capsules of absorbable materials such as gelatin.

[0088] Liquid compositions for oral administration include pharmacautically-acceptable emulsions, solutions, syrups and elixirs etc. In such liquid compositions, one or more of the active compound(s) is or are comprised in inert diluent(s) commonly used in tha art (for example, purified watar, ethanol etc.). Besides inert diluents, such compositions may also comprise adjuvants such as wetting agents, suspending agents, sweetening agents, flavouring agents, perfuming agants and preserving agents.

[0089] Other compositions for oral administration include spray compositions which may be prepared by known methods and which comprise one or more of the active compound(s). Spray compositions may comprise additional substances othar than inart diluents: a.g. stabilizing agents such as sodium hydrogan sulfata, stabilizing agents to give the title compound isotonicity, isotonic buffer such as sodium chloride, sodium citrate, citric acid. For preparation of such spray compositions, for example, the method described in the United States Patent No. 2868691 or 3095355 may be used.

[0090] Injections for parenteral administration include sterile aqueous or non-aqueous solutions, suspensions and emulsions. Aqueous solutions or suspensions includa distilled water for injection and physiological salt solution. Non-aqueous solutions or suspensions include propylane glycol, polyathylene glycol, plant oil such as olive oil, alcohol such as ethanol, POLYSORBATE80 (registered trade mark) etc. Such compositions may comprise additional diluents: e.g. preserving agents, wetting agents, emulsifying agents, dispersing agents, stabilizing agent, assisting agents such as assisting agents for dissolving (for example, glutamic acid, asparaginic acid). They may be sterilized for example, by filtration through a bacteria-retaining filter, by incorporation of sterilizing agents in the compositions or by irradiation. They also ba manufactured in the form of sfarile solid compositions and which can ba dissolved in sterile water or some othar starile diluents for injection immediately before used.

[0091] Other compositions for parenteral administration include liquids for external use, and endemic liniments, ointmant, suppositories and pessaries which comprise one or more of the active compound(s) and may be prepared by known methods.

Best mode to practica the invention

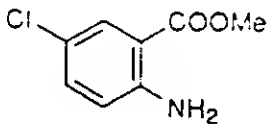
[0092] The following reference examples and examples are intended to illustrate, but not limit, the present invention.

[0093] The solvents in parentheses show the developing or eluting solvents and the ratios of the solvents used are by volume in chromatographic separations. Without special explanation, NMR data was determined in $CDCl_3$ solution.

Reference Example 1

5-chloro-anthranilic acid methyl ester

[0094]



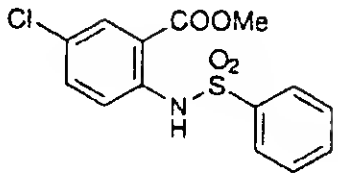
[0095] To e suspension of 5-chloroanthranilic acid (6 1 g) in AcOEt-MeOH (20 ml + 10 ml), a solution of an excess amount of diazomethane in ether (50 ml) was added at 0°C. After termination of reaction, reaction solvent was evaporated to dryness to give tha titla compound (6.6 g) having the following physicat data.

NMR : δ 7 82 (1H, d), 7.21 (1H, dd), 6.60 (1H, d), 5.73 (2H, brs), 3.88 (3H, s).

Reference Example 2

Methyl 2-phenylsulfonylamino-5-chlorobenzoate

[0096]



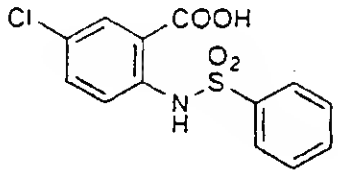
[0097] To a solution of 5-chloro-anthranilic acid methyl ester (400 mg; prepared in Reference Example 1.) and pyridine (0.87 ml) in methylene chloride, benzenesulfonylchloride (0.33 ml) was added at 0°C. The solution was stirred overnight at room temperature. The reaction mixture was poured into diluted HCl and extracted with ethyl acetate. The organic layer was washed, dried ovar and concentrated under reduced pressure. The rasidue was purified on silica gel column chromatography (hexane-AcOEt) to give the title compound (664 mg) having the following physical data.

TLC : Rf 0.30 (hexane : AcOEt = 4 : 1);
NMR: δ 10.5 (1H, s), 7.90-7.79 (3H, m), 7.79 (1H, d), 7.60-7.37 (4H, m), 3.88 (3H, s).

Reference Example 3

2-phenylsulfonylamino-5-chlorobenzoic acid

[0098]



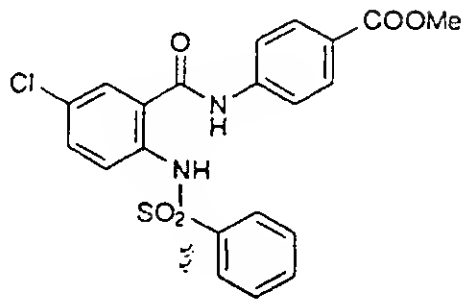
[0099] To a solution of methyl 2-phenylsulfonylamino-5-chlorobenzoate (600 mg; prepared in Reference Example 2.) in the mixture of THF-MeOH (6 ml + 3 ml), 2N NaOH solution (2 ml) was added. The mixture was stirred for 2 days. To the reaction mixtura, 1N HCl (4.5 ml) was added. Tha mixture was extracted with athyl acetate. The organic layer was washed and dried over to give the title compound (575 mg) having the following physical data.

NMR: δ 10.31 (1H, s), 7.99 (1H, d), 7.92-7.83 (2H, m), 7.70 (1H, d), 7.63-7.42 (4H, m), 6.20 (1H, brs).

Example 1

Methyl 4-(2-phenylsulfonylamino-5-chlorobenzoylamino)benzoate

[0100]



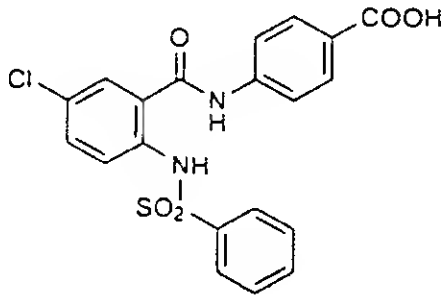
[0101] To a suspension of 2-phenylsulfonylamino-5-chlorobenzoic acid (250 mg; prepared in Reference Example 3.) and methyl p-aminobenzoate (133 mg) in methylene chloride (5 ml), EDC (168 mg) and dimethylaminopyridine (20 mg) were added. The mixture was stirred for 3 days at room temperature. The reaction mixture was poured into diluted HCl and extracted with ethyl acetate. The organic layer was washed, dried over and concentrated under reduced pressure. The residue was purified on silica gel column chromatography (AcOEt-benzene) to give the title compound (142 mg) having the following physical data.

TLC : Rf 0.29 (AcOEt : benzene = 1 : 9);
NMR ($CDCl_3$+DMSO-d_6) : δ 10.40 (1H, s), 9.90 (1H, m), 8.03 (2H, d), 7.82-7.70 (5H, m), 7.63 (1H, d), 7.50-7.24 (4H, m), 3.93 (3H, s).

Example 2

4-(2-phenylsulfonylamino-5-chlorobenzoylamino)benzoic acid

[0102]



[0103] To a solution of methyl 4-(2-phenylsulfonylamino-5-chlorobenzoylamino)benzoate (122 mg; prepared in Example 1.) in THF-MeOH (4 ml + 2 ml), 2N NaOH aqueous solution (0.5 ml) was added at room temperature. The mixture was stirred overnight. To the reaction mixture, 2N HCl (0.6 ml) and water were added. The mixture was extracted with ethyl acetate. The organic layer was washed, dried over and concentrated under reduced pressure. The residue was

purified by recrystallization from the mixture of AcOEt-hexane to give the title compound (80 mg) having the following physical data.

TLC : Rf 0.32 (MeOH : CH_2Cl_2 = 15 : 85);
NMR (DMSO-d_6) : δ 12.74 (1H, brs), 10.61 (1H, s), 10.40 (1H, s), 7.95 (2H, d), 7.85-7.71 (5H, m), 7.64-7.35 (5H, m).

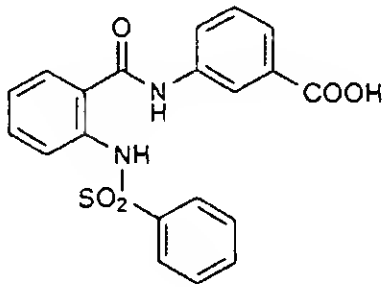
Example 2(a)-2(bb)

[0104] The title compounds having the following physical data were obtained by the same procedure of Reference Example 1~Reference Example 3 and Examples 1 and 2.

Example 2(a)

3-(2-phenylsulfonylaminobenzoylamino)benzoic acid

[0105]

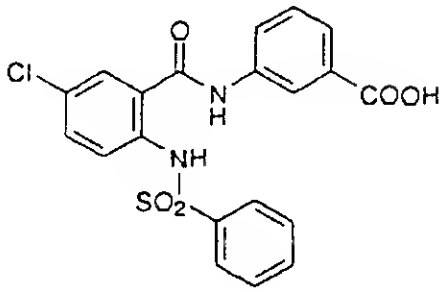


TLC : Rf 0.57 ($CHCl_3$: MeOH : AcOH= 100 : 10 : 1).
NMR (DMSO-d_6) : δ 13.01 (1H, brs), 10.66 (1H, brs), 10.50 (1H, brs), 8.32 (1H, brs), 7.89 (1H, d), 7.76 (4H, m), 7.51 (6H, m), 7.23 (1H, m).

Example 2(b)

3-(2-phenylsulfonylamino-5-chlorobenzoylamino)benzoic acid

[0106]

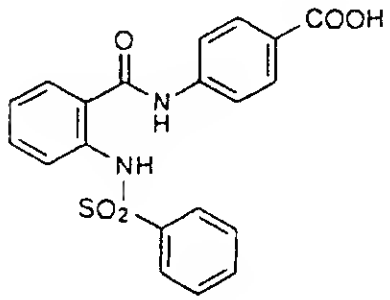


TLC : Rf 0.26 (MeOH : $CHCl_3$ = 15 : 85);
NMR ($CDCl_3$: DMSO-d_6=1:1) : δ 12.70 (1H, brs), 10.69 (1H, s), 10.44 (1H, s), 8.27 (1H, t), 7.95-7.69 (5H, m), 7.59-7.36 (6H, m).

Example 2(c)

4-(2-phenylsulfonylaminobenzoylamino)benzoic acid

[0107]

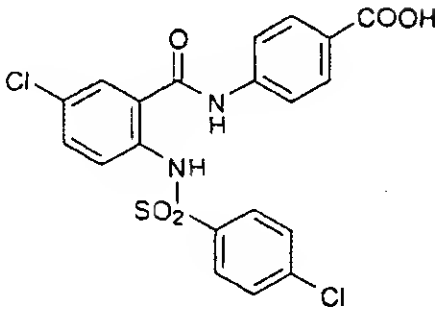


TLC Rf 0.50 ($CHCl_3$ · MeOH · AcOH= 100 · 10 : 1);
NMR (DMSO-d_6) : δ 12.76 (1H, brs), 10.57 (1H, s), 10.49 (1H, s), 7.95 (2H, d), 7.77 (5H, m), 7.28-7.62 (5H, m), 7.24 (1H, m).

Example 2(d)

4-[2-(4-chlorophenyl)sulfonylamino-5-chlorobenzoylamino]benzoic acid

[0108]

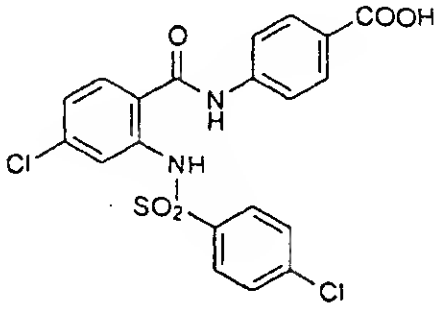


TLC : Rf 0.27 (MeOH : $CHCl_3$ = 15 : 85);
NMR (DMSO-d_6) : δ 12.70 (1H, br s), 10.59 (1H, s), 10.30 (1H, s), 7.95 (2H, d), 7.83-7.66 (5H, m), 7.62-7.47 (3H, m), 7.34 (1H, d).

Example 2(e)

4-[2-(4-chlorophenylsulfonylamino)-4-chlorobenzoylamino]benzoic acid

[0109]

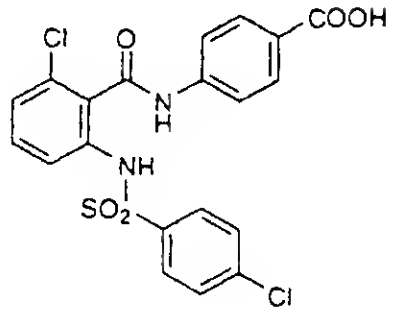


TLC : Rf 0.69 ($CHCl_3$: MeOH : AcOH= 17 : 2 : 1).
NMR ($CDCl_3$+DMSO-d_6) : δ 10.9-10.3 (1H, br), 10.3-9.9 (1H, br), 7.84 (2H, d), 7.7-7.5 (5H, m), 7.45 (1H, s-like), 7.17 (2H, d), 7.0-6.9 (1H, m).

Example 2(f)

4-[2-(4-chlorophenylsulfonylamino)-6-chlorobenzoylamino]benzoic acid

[0110]

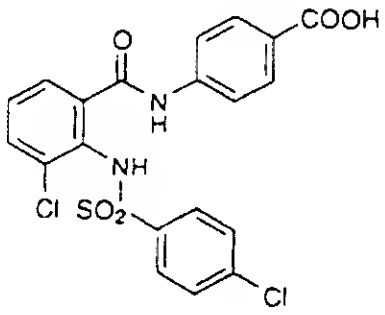


TLC : Rf 0.67 ($CHCl_3$: MeOH : AcOH= 17 : 2 : 1);
NMR : δ 9.64 (1H, s-like), 7.8-7.7 (2H, m), 7.5-7.3 (4H, m), 7.1-6.9 (5H, m).

Example 2(g)

4-[2-(4-chlorophenylsulfonylamino)-3-chlorobenzoylamino]benzoic acid

[0111]

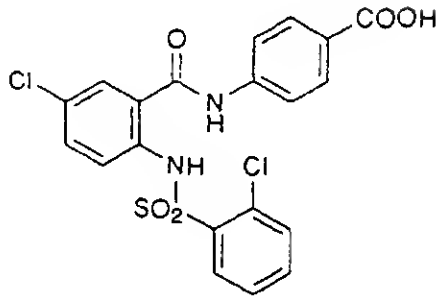


TLC Rf 0.32 ($CHCl_3$: MeOH = 9 : 1);
NMR (DMSO-d_6) : δ 12.8-12.6 (1H, br), 10.7-10.5 (1H, br), 10.12 (1H, s), 7.89 (2H, d), 7.7-7.5 (6H, m), 7.5-7.3 (3H, m).

Example 2(h)

4-[2-(2-chlorophenylsulfonylamino)-5-chlorobenzoylamino]benzoic acid

[0112]

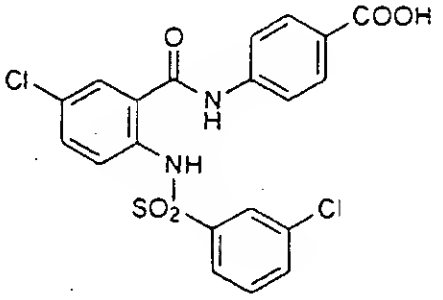


TLC : Rf 0.16 ($CHCl_3$: MeOH = 9 : 1);
NMR (DMSO-d_6) : δ 12.78 (1H, br), 10.80 (2H, br), 8.08-8.03 (1H, m),7.95 (2H, d), 7.88 (1H, d), 7.80 (2H, d), 7.66-7.46 (4H, m), 7.38 (1H, d).

Example 2(i)

4-[2-(3-chlorophenylsulfonylamino)-5-chlorobenzoylamino]benzoic acid

[0113]

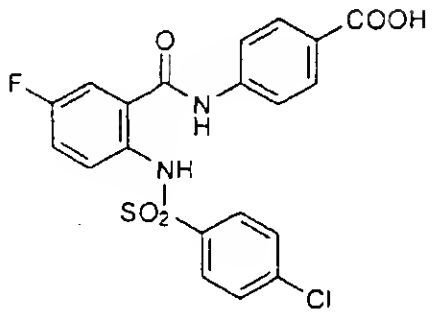


TLC : Rf 0.15 ($CHCl_3$: MeOH = 9 : 1);
NMR (DMSO-d_6) : δ 12.76 (1H, br), 10.62 (1H, brs), 10.36 (1H, brs), 7.92 (2H, d), 7.77-7.73 (4H, m), 7.67-7.44 (4H, m), 7.28 (1H, d).

Example 2(j)

4-[2-(4-chlorophenylsulfonylamino)-5-fluorobenzoylamino]benzoic acid

[0114]

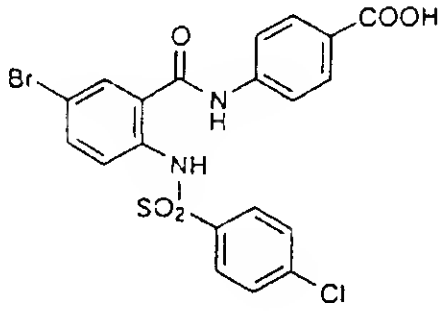


TLC . Rf 0.28 (MeOH : $CHCl_3$ = 15 : 85),
NMR (DMSO-d_6) : δ 12.78 (1H, brs), 10.50 (1H, s), 10.09 (1H, s), 7.95 (2H, d), 7.75 (2H, d), 7.68-7.26 (7H, m).

Example 2(k)

4-[2-(4-chlorophenylsulfonylamino)-5-bromobenzoylamino]benzoic acid

[0115]

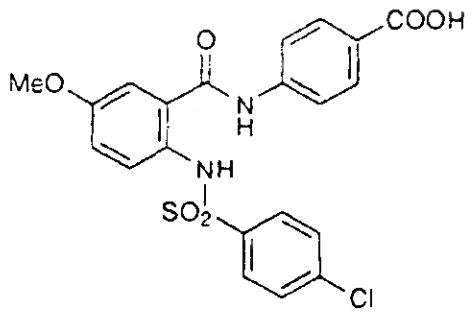


TLC Rf 0.28 (MeOH : $CHCl_3$ = 15 . 85).
NMR (DMSO-d_6) δ 12.74 (1H, brs), 10 61 (1H, s), 10 33 (1H, s), 7 95 (2H, d), 7.89 (1H, d), 7.81-7.65 (5H, m), 7.53 (2H, d), 7 29 (1H, d).

Example 2(l)

4-[2-(4-chlorophenylsulfonylamino)-5-methoxybenzoylamino]benzoic acid

[0116]

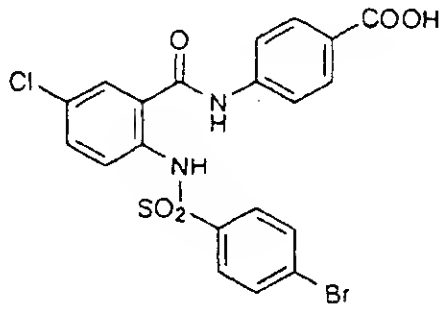


TLC : Rf 0.30 (MeOH : $CHCl_3$ = 15 : 85);
NMR (DMSO-d_6) : δ 12.77 (1H, brs), 10.39 (1H, s), 9.79 (1H, s), 7.94 (2H, d), 7.73 (2H, d), 7.59 (2H, d), 7.43 (2H, d), 7.25-7.15 (2H, m), 7.09 (1H, dd).

Example 2(m)

4-[2-(4-bromophenylsulfonylamino)-5-chlorobenzoylamino]benzoic acid

[0117]

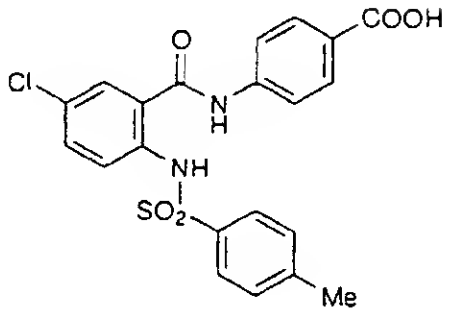


TLC : Rf 0.27 ($CHCl_3$: MeOH = 9 : 1);
NMR (DMSO-d_6) : δ 12.74 (1H, br), 10.55 (1H, brs), 10.27 (1H, brs), 7.92 (2H, d), 7.75-7.71 (3H, m), 7.66-7.51 (5H, m), 7.31 (1H, d).

Example 2(n)

4-[2-(4-methylphenylsulfonylamino)-5-chlorobenzoylamino]benzoic acid

[0118]

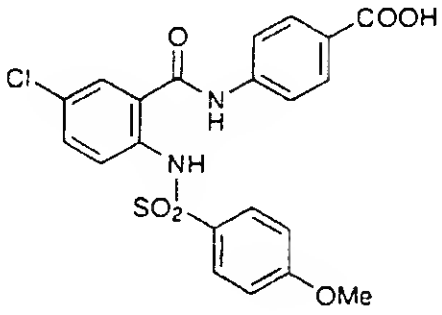


TLC Rf 0.30 ($CHCl_3$: MeOH = 9 : 1);
NMR (DMSO-d_6) : δ 12.76 (1H, br), 10.56 (1H, brs), 10.23 (1H, brs), 7.93 (2H, d), 7.77-7.73 (3H, m), 7.60-7.51 (3H, m), 7.36 (1H, d), 7.23 (2H, d), 2.24 (3H, s).

Example 2(o)

4-[2-(4-methoxyphenylsulfonylamino)-5-chlorobenzoylamino]benzoic acid

[0119]

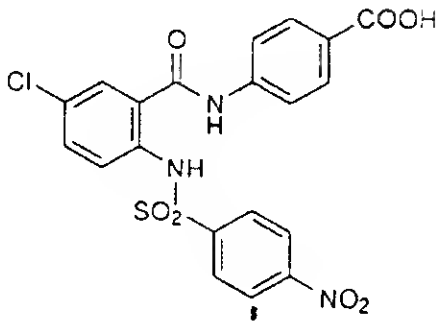


TLC Rf 0.29 ($CHCl_3$: MeOH = 9 : 1);
NMR (DMSO-d_6) : δ 12.76 (1H, br), 10.57 (1H, brs), 10.16 (1H, brs), 7.93 (2H, d), 7.77-7.73 (3H, m), 7.62 (2H, d), 7.59-7.52 (1H, m), 7.37 (1H, d), 6.93 (2H, d), 3.70 (3H, s).

Example 2(p)

4-[2-(4-nitrophenylsulfonylamino)-5-chlorobenzoylamino]benzoic acid

[0120]

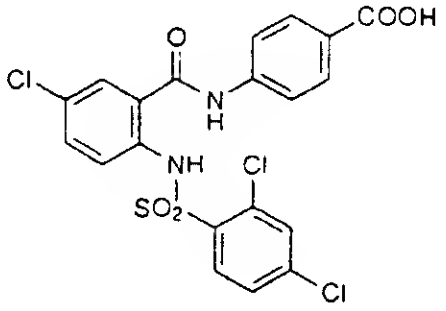


TLC : Rf 0.10 ($CHCl_3$: MeOH = 9 : 1);
NMR (DMSO-d_6) : δ 12.71 (1H, br), 10.55-10.35 (2H, br), 8.19 (2H, d), 7.93-7.86 (4H, m), 7.71-7.64 (3H, m), 7.58-7.52 (1H, m), 7.32 (1H, d).

Example 2(q)

4-[2-(2,4-dichlorophenylsulfonylamino)-5-chlorobenzoylamino]benzoic acid

[0121]

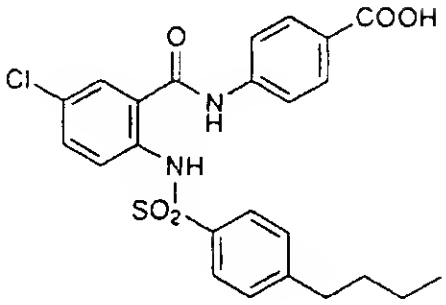


TLC : Rf 0.22 ($CHCl_3$: MeOH = 9 : 1);
NMR (DMSO-d_6) : δ 12.50 (1H, br), 10.73 (2H, br), 7.99-7.91 (3H, m), 7.85 (1H, d-like), 7.79-7.71 (3H, m), 7.58-7.51 (2H, m), 7.36 (1H, d).

Example 2(r)

4-[2-(4-butylphenylsulfonylamino)-5-chlorobenzoylamino]benzoic acid

[0122]

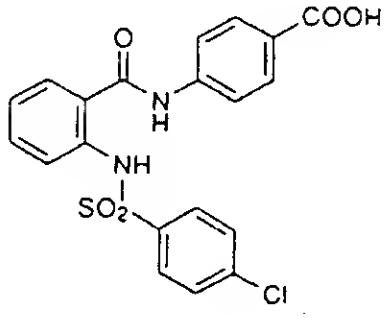


TLC : Rf 0.33 ($CHCl_3$: MeOH = 9 : 1);
NMR (DMSO-d_6) : δ 12.72 (1H, br), 10.55 (1H, brs), 10.24 (1H, s), 7.92 (2H, d), 7.78-7.72 (3H, m), 7.60 (2H, d), 7.57-7.51 (1H, m), 7.37 (1H, d), 7.24 (2H, d), 2.54-2.49 (2H, m), 1.48-1.33 (2H, m), 1.29-1.11 (2H, m), 0.82 (3H, t).

Example 2(s)

4-[2-(4-chlorophenylsulfonylamino)benzoylamino]benzoic acid

[0123]

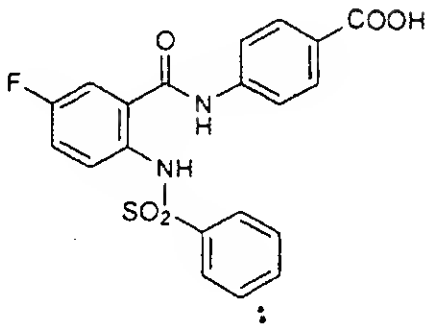


TLC : Rf 0.30 (AcOEt : hexane : AcOH= 7 : 16 : 1);
NMR (DMSO-d_6) : δ 13.00-12.60 (1H, brs), 10.55 (1H, brs), 10.38 (1H, brs), 7.95 (2H, d), 7.78 (2H, d), 7.74 (1H, m), 7.72 (2H, d), 7.51 (2H, d), 7.50 (1H, m), 7.40-7.24 (2H, m).

Example 2(t)

4-(2-phenylsulfonylamino-5-fluorobenzoylamino)benzoic acid

[0124]

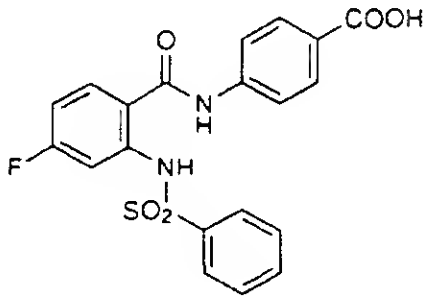


TLC : Rf 0.23 ($CHCl_3$: MeOH = 9 : 1);
NMR ($DMSO-d_6$) : δ 12.70 (1H, br), 10.52 (1H, br), 10.13 (1H, br), 7.92 (2H, d), 7.74 (2H, d), 7.68-7.64 (2H, m), 7.59-7.27 (6H, m)

Example 2(u)

4-(2-phenylsulfonylamino-4-fluorobenzoylamino)benzoic acid

[0125]

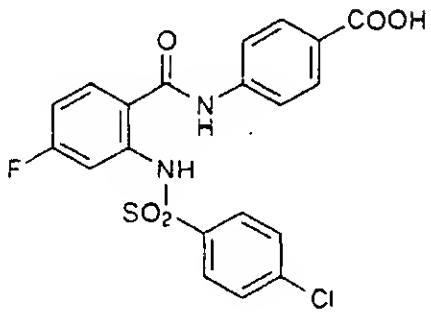


TLC : Rf 0.20 ($CHCl_3$: MeOH = 9 : 1),
NMR ($DMSO-d_6$) : δ 12.81 (1H, br), 10.85 (1H, br), 10.60 (1H, br), 7.95-7.74 (7H, m), 7.63-7.46 (3H, m), 7.19-7.02 (2H, m).

Example 2(v)

4-[2-(4-chlorophenylsulfonylamino)-4-fluorobenzoylamino]benzoic acid

[0126]

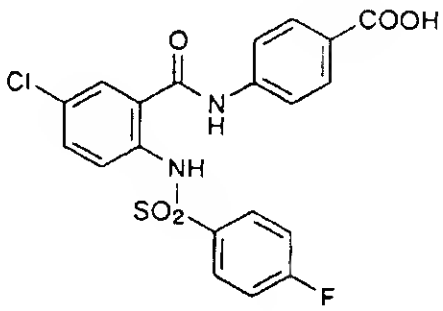


TLC : Rf 0.22 ($CHCl_3$: MeOH = 9 : 1);
NMR (DMSO-d_6) : δ 12.28 (1H, br), 10.75 (1H, br), 10.58 (1H, br), 7.95-7.72 (7H, m), 7.53 (2H, d), 7.19-7.08 (2H, m).

Example 2(w)

4-[2-(4-fluorophenylsulfonylamino)-5-chlorobenzoylamino]benzoic acid

[0127]

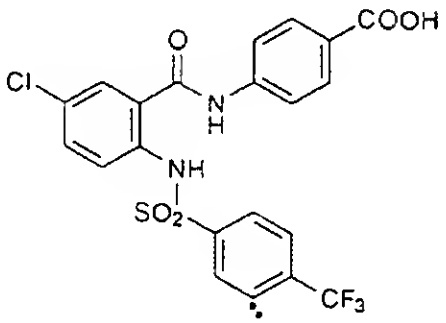


TLC Rf 0.26 ($CHCl_3$: MeOH = 9 : 1);
NMR (DMSO-d_6) : δ 12.75 (1H, br), 10.58 (1H, br), 10.27 (1H, brs), 7.93 (2H, d), 7.80-7.72 (5H, m), 7.54 (1H, dd), 7.34-7.22 (3H, m).

Example 2(x)

4-[2-(4-trifluoromethylphenylsulfonylamino)-5-chlorobenzoylamino]benzoic acid

[0128]

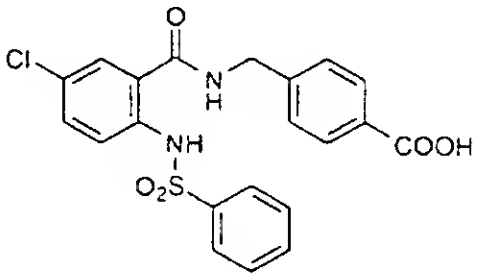


TLC : Rf 0.26 ($CHCl_3$: MeOH = 9 : 1);
NMR (DMSO-d_6) : δ 12.70 (1H, br), 10.56 (1H, br), 10.41 (1H, br), 7.92-7.68 (9H, m), 7.54 (1H, dd-like), 7.31 (1H, d).

Example 2(y)

4-(2-phenylsulfonylamino-5-chlorobenzoylaminomethyl)benzoic acid

[0129]

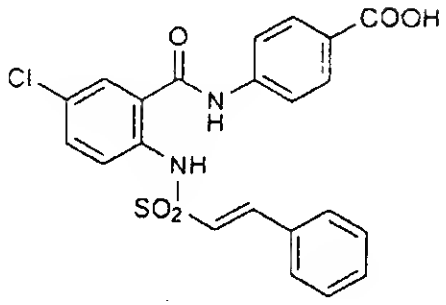


TLC : Rf 0.45 (MeOH : $CHCl_3$ = 1 : 4),
NMR (DMSO-d_6) : δ 12.90 (1H, s), 11.47 (1H, s), 9.46 (1H, t), 7.94 (2H, d), 7.86 (1H, d), 7.77-7.36 (9H, m), 4.48 (1H, d).

Example 2(z)

4-[2-(2-phenylvinyl)sulfonylamino-5-chlorobenzoylamino]benzoic acid

[0130]

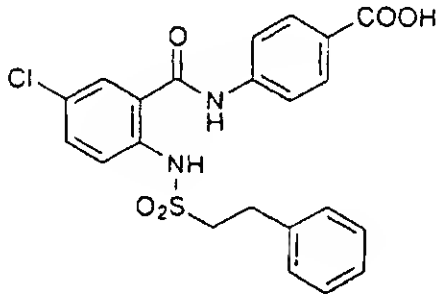


TLC : Rf 0.43 ($CHCl_3$: MeOH = 9 : 1);
NMR (CD_3OD) : δ 7.98 (2H, d), 7.83 (1H, d), 7.72 (2H, d), 7.63 (1H, d), 7.53 (1H, dd), 7.5-7.2 (6H, m), 7.01 (1H, d).

Example 2(aa)

4-[2-(2-phenylethyl)sulfonylamino-5-chlorobenzoylamino]benzoic acid

[0131]

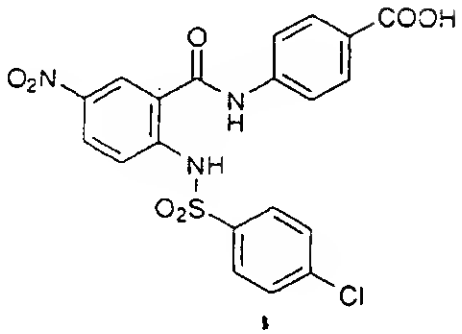


TLC Rf 0.27 ($CHCl_3$. MeOH = 9 : 1),
NMR (DMSO-d_6) : δ 12.75 (1H, br), 10.78 (1H, brs), 10.05 (1H, s), 7.95-7.79 (5H, m), 7.63-7.53 (2H, m), 7.24-7.10 (5H, m), 3.53-3.45 (2H, m), 2.99-2.91 (2H, m)

Example 2(bb)

4-[2-(4-chlorophenylsulfonylamino)-5-nitrobenzoylamino]benzoic acid

[0132]

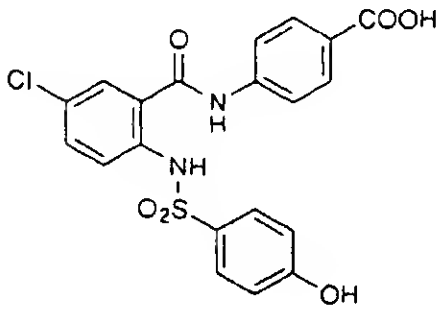


TLC : Rf 0.32 (AcOEt : hexane : AcOH= 4 : 12 : 1);
NMR (DMSO-d_6) : δ 12.50-10.00 (2H, brs), 8.66 (1H, d), 8.36-8.24 (1H, dd), 8.05-7.87 (4H, m), 7.80 (2H, d), 7.68-7.55 (3H, m).

Example 3

4-[2-(4-hydroxyphenylsulfonylamino)-5-chlorobenzoylamino]benzoic acid

[0133]



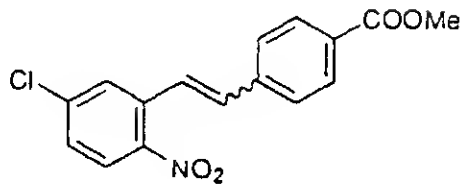
[0134] To a mixture solution of methyl 4-[2-(4-pivaroyloxyphenylsulfonylamino)-5-chlorobenzoylamino]benzoate (214 mg; prepared by the same procedure as Reference Examples 1, 2 and 3 and Example 1.) in MeOH-THF (8 ml + 3 ml), 2N NaOH aqueous solution (2 ml) was added The mixture was stirred for one day at 60°C. To the reaction solution, HCl was added The mixture was extracted with ethyl acetate. The organic layer was washed, dried over and purified by recrystallization from the mixture solvent of MeOH-AcOEt·hexane to give the title compound (105 mg) having the following physical data.

TLC : Rf 0.42 ($CHCl_3$: MeOH : AcOH= 45 : 4 : 1);
NMR (DMSO-d_6) : δ 13.0-12.6 (1H, br), 10.64 (1H, s-like), 10.50 (1H, s-like), 10.21 (1H, s), 7.95 (2H, d), 7.9-7.7 (3H, m), 7.6-7.3 (4H, m), 6.76 (2H, d).

Reference Example 4

Methyl 4-[2-(2-nitro-5-chlorophenyl)-(EZ)-vinyl]benzoate

[0135]



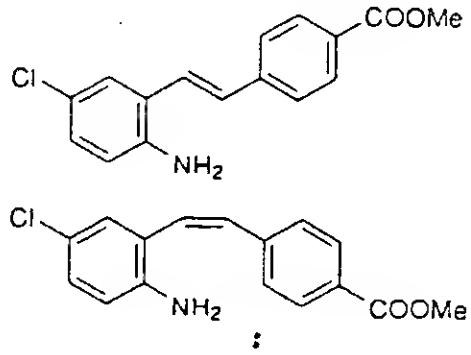
[0136] To e solution of 4-methoxycarbonylphenylmethyltriphenylphosphine bromide (4.83 g) in THF (20 ml), potassium t-butoxide (600 mg) was added. The mixture was stirred for 1 hour at room temperature. To the reaction solution, 2-nitro-5-chlorobenzaldehyde (742 mg) was added at 0°C. The mixture was stirred for 30 minutes at room temperature. The reaction mixture was poured into diluted HCl. The mixture was extracted with hexane-AcOEt. The organic layer was weshed, dried over end concentrated under the reduced pressure. The residue was purified on silica gel column chromatography (hexane-AcOEt) and recrystallization from the mixture solvent of hexane-AcOEt to give the title compound (680 mg) having the following physical data.

TLC : Rf 0.44 (hexane : AcOEt = 4 : 1).

Reference Example 5

Methyl 4-[2-(2-amino-5-chlorophenyl)-(E)-vinyl]benzoate and methyl 4-[2-(2-amino-5-chlorophenyl)-(Z)-vinyl]benzoate

[0137]



[0138] To e solution of methyl 4-[2-(2-nitro-5-chlorophenyl)-(EZ)-vinyl]benzoate (525 mg; prepared in Reference Example 4.) in THF (4 ml), water (1.5 ml), 2N HCl and reduced iron (554 mg) were added. The mixture was stirred overnight at room temperature. Further, to the mixture, 2N HCl (0.2 ml) and reduced iron powder (330 mg) were added. The mixture wes stirred for 3 days. The reection mixture wes diluted with ethyl ecetete end filtreted. The filtrate was weshed, dried over end concentrated under the reduced pressure. The residue was purified on silica gel column chromatography (ether-hexane-AcOEt) to give the title compound having the following physical data.

(E) type compound

[0139]

TLC : Rf 0.37 (AcOEt : benzene = 5 : 95).

(Z) type compound

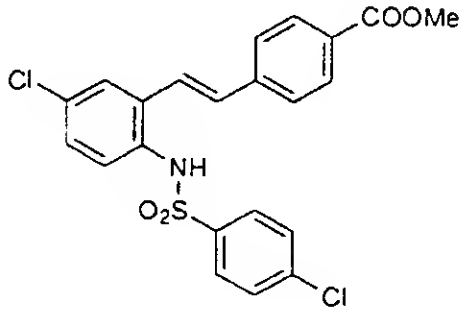
[0140]

TLC : Rf 0.41 (AcOEt : benzene = 5 : 95).

Example 4

Methyl 4-[2-[2-(4-chlorophenylsulfonylamino)-5-chlorophenyl]-(E)-vinyl]benzoate

[0141]



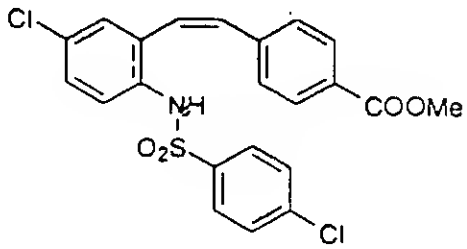
[0142] To methyl 4-[2-(2-amino-5-chlorophenyl)-(E)-vinyl]benzoate (130 mg; prepared in Reference Example 5.) in methylene chloride (3 ml), pyridine (0.073 µl) and p-chlorobenzenesulfonylchloride (114 mg) were added. The mixture was stirred overnight et room tempereture. The reaction mixture was poured into diluted HCl and extracted with ethyl acetate. The organic layer was washed, dried over and concentrated under the reduced pressure. The residue was purified on silica gel column chromatography (AcOEt-hexane) to give the title compound (205 mg) having the following physical data.

TLC : Rf 0.15 (AcOEt : benzene = 4 : 96);
NMR : δ 8.02 (2H, d), 7.63 (2H, d), 7.51 (1H, s), 7.41-7.30 (4H, m), 7.26-7.22 (2H, m), 6.91 (1H, d), 6.81 (1H, d), 6.63 (1H, s), 3.95 (3H, s).

Example 4(a)

Methyl 4-[2-[2-(4-chlorophenylsulfonylamino)-5-chlorophenyl]-(Z)-vinyl]benzoate

[0143]



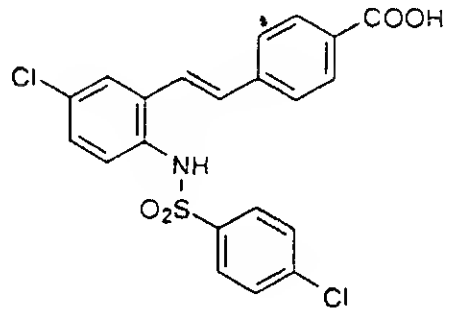
[0144] By using Z type compound prepared in Reference Example 5, the title compound having the following physical data was obtained by the same procedure as Example 4.

TLC : Rf 0.23 (AcOEt : benzene = 4 : 96);
NMR : δ 7.82 (2H, d), 7.57 (2H, d), 7.46 (1H, d), 7.33 (2H, d), 7.24 (1H, dd), 7.06 (1H, d), 6.99 (2H, d), 6.72 (1H, d), 6.48 (1H, s), 6.20 (1H, d), 3.90 (3H, s).

Example 5

4-[2-[2-(4-chlorophenylsulfonylamino)-5-chlorophenyl]-(E)-vinyl]benzoic acid

[0145]



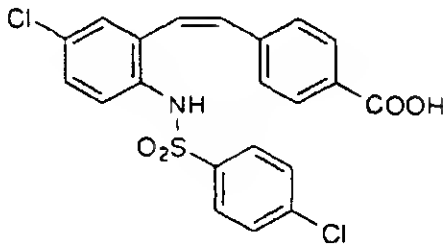
[0146] By using methyl 4-[2-[2-(4-chlorophenylsulfonylamino)-5-chlorophenyl]-(E)-vinyl]benzoate (190 mg; prepared in Example 4.), the title compound (168 mg) having the following physical data was obtained by the same procedure as Example 2.

TLC : Rf 0.36 (MeOH : $CHCl_3$ = 15 : 85);
NMR (DMSO-d_6) : δ 10.11 (1H, brs), 7.96 (2H, d), 7.80 (1H, d), 7.59 (2H, d), 7.52-.7.41 (4H, m), 7.36 (1H, dd), 7.20 (1H, d), 7.15 (1H, d), 7.08 (1H, d).

Example 5(a)

4-[2-[2-(4-chlorophenylsulfonylamino)-5-chlorophenyl]-(Z)-vinyl]benzoic acid

[0147]



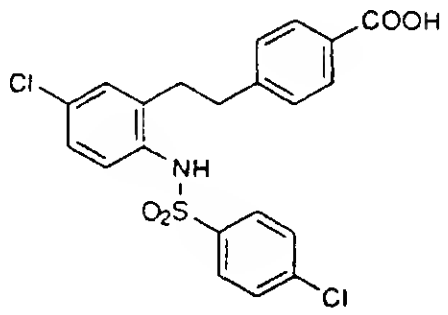
[0148] By using methyl 4-[2-[2-(4-chlorophanylsulfonylamino)-5-chlorophenyl]-(Z)-vinyl]benzoate prepared in Example 4(a), the title compound having the following physical data was obtained by the same procedure as Example 2.

TLC : Rf 0.46 ($MeOH : CHCl_3$ = 15 : 85);
NMR ($DMSO-d_6$) : δ 10.05 (1H, brs), 7.79-7.67 (4H, m), 7.55 (2H, d), 7.30 (1H, dd), 7.15 (1H, d), 7.00 (1H, d), 6.91 (1H, d), 6.64 (2H, s).

Example 6

4-[2-[2-(4-chlorophenyl)sulfonylemino-5-chlorophenyl]ethyl]benzoic ecid

[0149]



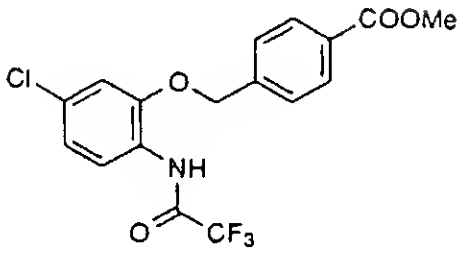
[0150] To e solution of 4-[2-[2-(4-chlorophenyl)sulfonylamino-5-chlorophenyl]vinyl]benzoic acid (54 mg; prepared in Example 5.) in THF (4 ml), platinum oxide hydrate (3 mg) was added. The mixture was stirred for 2 hours at room temperetune in e stream of hydrogen. The reaction mixture was filtered and the filtrate was concentrated under the reduced pressure. To the residue, methylene chloride was added The mixture was stirred. The precipitate was collected by filter to give the title compound (46 mg) having the following physical data.

TLC : Rf 0.42 ($MeOH : CHCl_3$ = 15 : 85);
NMR ($DMSO-d_6$) : δ 12.75 (H, s), 9.88 (1H, s), 7.84 (2H, d), 7.72-7.57 (4H, m), 7.32 (1H, d), 7.23 (2H, d), 7.18 (1H, dd), 6.88 (1H, d).

Reference Example 6

Methyl 4-(2-trifluoroacetylamino-5-chlorophenoxymethyl)b nzoate

[0151]



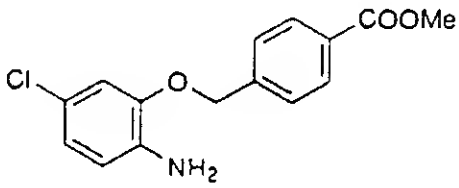
[0152] To a solution of 2-trifluoroacetylamino-5-chlorophenol (350 mg) and methyl 4-bromomethylbenzoate (435 mg) in DMF (3 ml), potassium carbonate (263 mg) was added at room temperature. The mixture was stirred for 1.5 hours at 60°C After the termination of reection, the reaction mixture wes poured into diluted HCl end extracted with ethyl acetate. The organic layer was washed, dried over and concentrated under the reduced pressure. The residue was purified on silica gel column chromatography (AcOEt-benzene) to give the title compound (353 mg) having the following physical dete

TLC . Rf 0.44 (AcOEt : benzene = 5 : 95).

Reference Example 7

Methyl 4-(2-amino-5-chlorophenoxymethyl)benzoate

[0153]



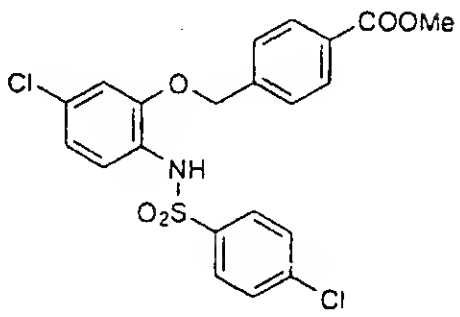
[0154] To a solution of methyl 4-(2-trifluoroacetylamino-5-chlorophenoxymethyl)benzoate (300 mg; prepared in Reference Exemple 6.) in mixture of THF-MeOH (4 ml + 10 ml), e solution of sodium carbonate (440 mg) in weter (2 ml) was added. The solution was stirred for 8 hours at 60°C and overnight at room temperature. The reaction mixture was poured into diluted HCl and extracted with ethyl acetate. The organic layer was washed, dried over and concentrated under the reduced pressure. The residue was purified on silica gel column chromatography (AcOEt-benzene) to give the title compound (194 mg) having the following physical data.

TLC : Rf 0.27 (AcOEt : benzene = 5 : 95).

Example 7

Methyl 4-[2-(4-chlorophanylsulfonylamino)-5-chlorophenoxymathyl]banzoata

[0155]



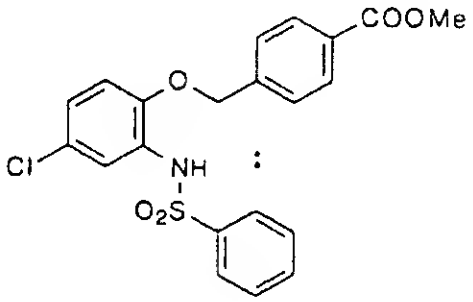
[0156] By using methyl 4-(2-amino-5-chlorophenoxymethyl)benzoate (165 mg; prepared in Reference Example 7.), the title compound (259 mg) having the following physical data was obtained by tha same procedura as Example 4.

TLC : Rf 0.30 (AcOEt : benzena = 5 : 95);
NMR : δ 8.06 (2H, d), 7.59 (2H, d), 7.53 (1H, d), 7.34 (2H, d), 7.18 (2H, d), 6.96 (1H, dd), 6.82 (1H, brs), 6.76 (1H, d), 4.89 (2H, s), 3.96 (3H, s).

Example 7(a)

Methyl 4-(2-phenylsulfonylamino-4-chlorophenoxymethyl)benzoate

[0157]



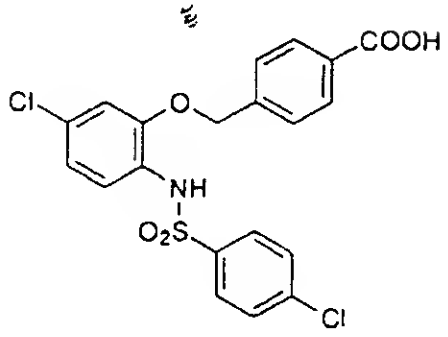
[0158] By using 2-trifluoroacetylamino-4-chlorophenol, the title compound having the following physical data was obtained by the same procedure as Reference Example 6→Reference Example 7→Example 4→Example 2.

TLC : Rf 0.37 (hexana : AcOEt = 2 : 1);
NMR : δ 8.01 (2H, d, J=8.4Hz), 7.75 (2H, m), 7.63 (1H, d, J=2 4Hz), 7.56 (1H, m), 7.43 (2H, m), 7.15 (2H, d, J=8.4Hz), 6.69 (1H, brs), 6.97 (1H, dd, J=2.4, 8.8Hz), 6.63 (1H, d, J=8.8Hz), 4.92 (2H, s), 3.94 (3H, s).

Example 8

4-[2-(4-chlorophenylsulfonylamino)-5-chlorophenoxymethyl]benzoic acid

[0159]



[0160] By using methyl 4-[2-(4-chlorophenylsulfonylamino)-5-chlorophenoxymethyl]benzoate (210 mg; prepared in Example 7.), the title compound (197 mg) having the following physical data was obtained by the same procedure as Example 2.

TLC : Rf 0.43 (MeOH : $CHCl_3$ = 15 : 85);
NMR (DMSO-d_6) : δ 9.89 (1H, br s), 7.93 (2H, d), 7.60 (2H, d), 7.42 (2H, d), 7.34 (2H, d), 7.29 (1H, d), 7.06 (1H, d), 7.01 (1H, dd), 4.98 (2 H, s).

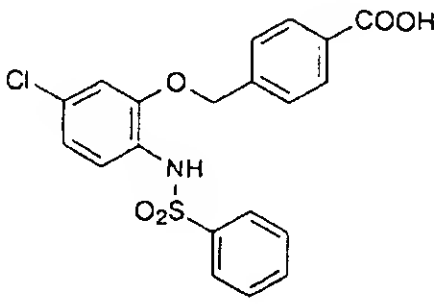
Example 8(a)-8(c)

[0161] The title compounds having the following physical data were obtained by the same procedure as Reference Examples 6, 7 and Examples 7 and 8.

Example 8(a)

4-(2-phenylsulfonylamino-5-chlorophenoxymethyl)benzoic acid

[0162]



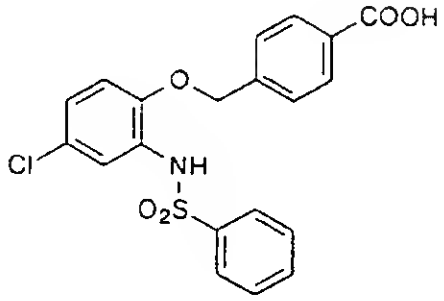
TLC : Rf 0.39 (MeOH : $CHCl_3$ = 2 : 8);
NMR (DMSO-d_6) : δ 12.98 (1H, s), 9.78 (1H, s), 7.92 (2H, d), 7.65 (2H, d), 7.55 (1H, t), 7.41 (2H, t), 7.37 (2H, d),

7.28 (1H, d), 7.04 (1H, dz), 6.98 (1H, dd), 4.98 (2H, s).

Example 8(b)

4-(2-phenylsulfonylamino-4-chlorophenoxymethyl)benzoic acid

[0163]

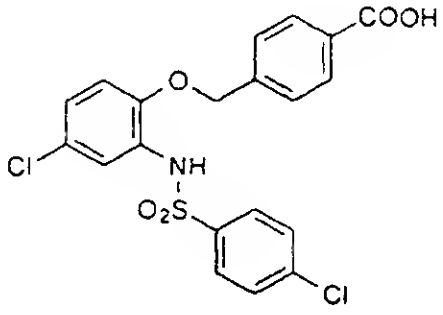


TLC : Rf 0.40 (MeOH : $CHCl_3$ = 2 : 8);
NMR (DMSO-d_6) : δ 12.98 (1H, brs), 9.94 (1H, s), 7.90 (2H, d), 7.70 (2H, d), 7.58 (1H, t), 7.44 (2H,), 7.36 (2H, d), 7.28 (1H, d), 7.15 (1H, dd), 6.94 (1H, d), 4.97 (2H, s).

Example 8(c)

4-[2-(4-chlorophenylsulfonylamino)-4-chlorophenoxymethyl]benzoic acid

[0164]

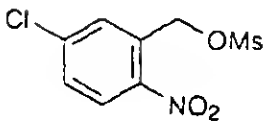


TLC : Rf 0.40 (MeOH : $CHCl_3$ = 2 : 8);
NMR (DMSO-d_6) . δ 12.93 (1H, s), 10.02 (1H, s), 7.88 (2H, d), 7.61 (2H, d), 7.42 (2H, d), 7.35-7.22 (3H, m), 7.17 (1H, dd), 6.93 (1H, d), 4.94 (2H, s).

Reference Example 8

O-mesyl-2-nitro-5-chlorobenzyl alcohol

[0165]



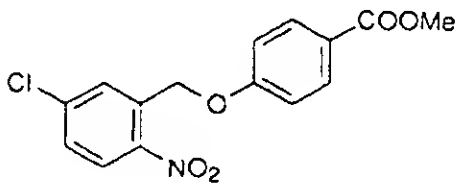
[0166] A solution of 2-nitro-5-chlorobenzyl alcohol (400 mg) in methylene chloride (6 ml) was cooled by salt-ice. To this solution, triethylamine(0.6 ml) and mesylchloride (0.25 ml) were added. The mixture was stirred for 15 minutes. To the reection mixture, water was added. The mixture wes extracted with ethyl acetate. The organic layer was weshed, dried over and concentrated under the reduced pressure to give the title compound (600 mg) having the following physical data.

TLC : Rf 0.36 (hexane : AcOEt = 2 : 1).

Reference Example 9

Methyl 4-(2-nitro-5-chlorophenylmethoxy)benzoate

[0167]



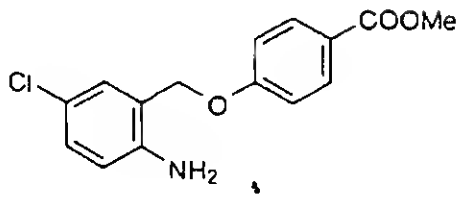
[0168] To a solution of O-mesyl-2-nitro-5-chlorobenzyl alcohol (600 mg; prepared in Reference Example 8.) in acetone (10 ml), methyl 4-hydroxybenzoate (425 mg) and potassium carbonate (900 mg) were added. The mixture was stirred for 1 hour To the reaction mixture, ecetone (10 ml) wes edded. The mixture was stirred for 22 hours end filtered. The filtrate was concentrated under the reduced pressure. The residue was purified on silica gel column chromatography (hexane-AcOEt) to give the title compound (463 mg) having the following physical data.

TLC : Rf 0.26 (hexane : AcOEt = 2 : 1).

Reference Example 10

Methyl 4-(2-amino-5-chlorophenylmethoxy)benzoate

[0169]



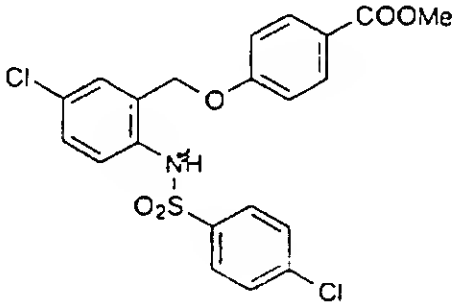
[0170] A mixture of methyl 4-(2-nitro-5-chlorophenylmethoxy)benzoate (460 mg; prepared in Reference Example 9.), THF (10 ml), water (3 ml), 1N HCl (0.4 ml) and iron powder (500 mg) was stirred for 13 hours. The reaction mixture was filtered. The filtrate was washed, dried over and concentrated under the reduced pressure. The residue was purified on silica gel column chromatography (hexane-AcOEt) to give the title compound (419 mg) having the following physical data.

TLC : Rf 0.23 (hexane : AcOEt = 4 : 1).

Example 9

Methyl 4-[2-(4-chlorophenylsulfonylamino)-5-chlorophenylmethoxy]benzoate

[0171]



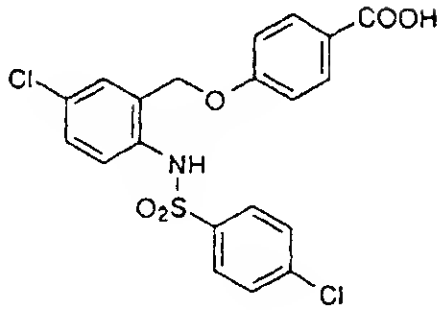
[0172] To a solution of methyl 4-(2-amino-5-chlorophenylmethoxy)benzoate (450 mg; prepared in Reference Example 10.) in methylene chloride (4 ml), pyridine (0.24 ml) and 4-chlorobenzenesulfonylchloride (380 mg) were added. The mixture was stirred for 21 hour. To the reaction mixture, water was added. The mixture was extracted with ethyl ecetate. The organic layer was washed, dried over end concentrated under the reduced pressure. The residue was purified by recrystallization from hexane-AcOEt mixture solvent to give the title compound (310 mg) having the following physical data.

TLC : Rf 0.45 (benzene : AcOEt = 9 : 1);
NMR : δ 8.01 (2H, d), 7.62 (2H, d), 7.40 (2H, d), 7.32-7.26 (3H, m), 7.11 (1H, brs), 6.90 (2H, d), 4.80 (2H, s), 3.90 (3H, s).

Example 10

4-[2-(4-chlorophenylsulfonylamino)-5-chlorophenylmethoxy]benzoic acid

[0173]



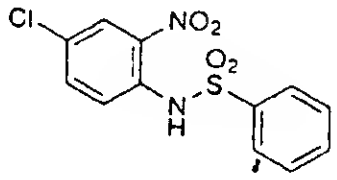
[0174] By using methyl 4-[2-(4-chlorophenylsulfonylamino)-5-chlorophenylmethoxy]benzoate (300 mg; prepared in Exemple 9.), the title compound (187 mg) having the following physical date was obtained by the seme procedure as Example 2.

TLC : Rf 0.51 (AcOEt);
NMR (DMSO-d_6) : δ 10.2-10.0 (1H, br), 7.90 (2H, d), 7.69 (2H, d), 7.61 (2H, d), 7.49 (1H, d), 7.36 (1H, dd), 7.01 (1H, d), 6.92 (2H, d), 5.02 (2H, s).

Reference Example 11

2-phenylsulfonylamino-5-chloro-1-nitrobenzene

[0175]



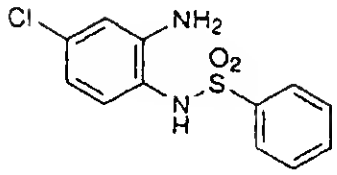
[0176] To a solution of 2-nitro-4-chloroaniline (500 mg) and pyridine (2.1 ml in methylene chloride (10 ml), benzenesulfonylchloride (1.2 ml) was edded dropwise et 0°C under en etmosphere of ergon. The reaction mixture wes stirred for 3 days at room temperature. To the reaction mixture, water was added. The mixture was extracted with ethyl acetate. The organic layer was washed, dried over and concentrated under the reduced pressure. The reside was recrystallized from AcOEt-hexene mixture solvent to give the by-product. The mother liquor was concentrated under the reduced pressure. The residue was purified on silica gel column chrometography (AcOEt-hexene) and recrystallized from AcOEt-hexane mixture solvent to give the title compound (175 mg) having the following physical data.

TLC . Rf 0.37 (AcOEt : hexene = 1 : 5).

Reference Example 12

2-phenylsulfonylamino-5-chloroaniline

[0177]



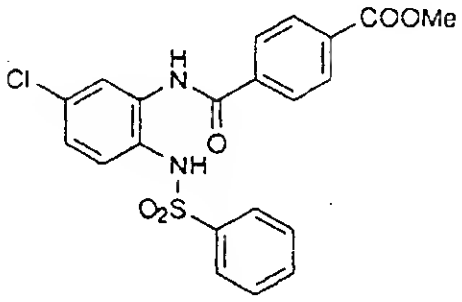
[0178] To a solution of 2-phenylsulfonylamino-5-chloro-1-nitrobenzene (172 mg; prepared in Reference Example 11.) in acetic acid (4 ml), reduced iron powder (154 mg) was added at room temperature under an atmosphere of argon. The suspension was stirred for 2 hours at 120°C. The reaction suspension was diluted with ethyl acetate and filtered. The filtrate was concentrated under the reduced pressure. The residue was purified on silica gel column chromatography (AcOEt-hexane) to give the title compound (92 mg) having the following physical data.

TLC : Rf 0.34 (AcOEt : hexane = 1 : 2).

Example 11

Methyl 4-(2-phenylsulfonylamino-5-chlorophenylaminocarbonyl)benzoate

[0179]



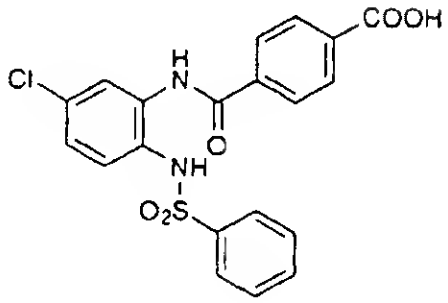
[0180] To a solution of 2-phenylsulfonylamino-5-chloroaniline (90 mg; prepared in Reference Example 12.) and pyridine (0.05 ml) in methylene chloride (5 ml), 4-methoxycarbonylbenzoic acid chloride (70 mg) was added at room temperature in a stream of argon. The mixture was stirred for 6 hours. After the termination of reaction, water was added to the reaction mixture. The mixture was extracted with ethyl acetate. The organic layer was washed, dried over and concentrated under the reduced pressure. The residue was purified by the recrystallization from AcOEt-hexane mixture solvent to give the title compound (112 mg) having the following physical data.

TLC : Rf 0.55 (AcOEt : hexane = 1 : 1);
NMR ($CDCl_3$+DMSO-d_6) : δ 9.41 (1H, brs), 8.93 (1H, brs), 8.22 (1H, d), 8.15 (2H, d), 7.98 (2H, d), 7.72-7.62 (2H, m), 7.58-7.45 (1H, m), 7.44-7.32 (2H, m), 6.96 (1H, dd), 6.82 (1H, d).

Example 12

4-(2-phenylsulfonylamino-5-chlorophenylaminocarbonyl)benzoic acid

[0181]



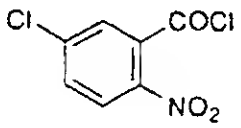
[0182] By using methyl 4-(2-phenylsulfonylamino-5-chlorophenylaminocarbonyl)benzoate (110 mg; prepared in Example 11.), the title compound (107 mg) having the following physical data was obtained by the same procedure as Example 2.

TLC : Rf 0.36 (AcOEt : hexane : AcOH= 8 : 10 : 1);
NMR (DMSO-d_6) : δ 13.00 (1H, brs), 9.80 (1H, brs), 9.65 (1H, s), 8.09 (2H, d), 7.87 (2H, d), 7.81 (1H, d), 7.65-7.50 (3H, m), 7.40 (2H, t), 7.22 (1H, dd), 7.14 (1H, d).

Reference Example 13

2-nitro-5-chlorobenzoic acid chloride

[0183]

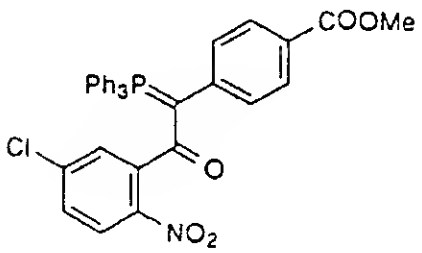


[0184] A solution of 2-nitro-5-chlorobenzoic acid (200 mg) in sulfonylchloride (20 ml) was stirred for 4 hours at 99°C in a stream of argon. After leaving to cool, the solution was concentrated under the reduced pressure to give the title compound

Reference Example 14

1-(2-nitro-5-chlorobenzoyl)-1-(4-methoxycarbonylphenyl)methylidene triphenylphosphoran

[0185]



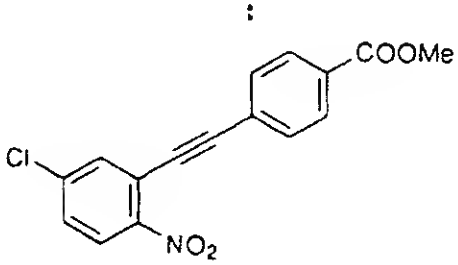
[0186] To a solution of 4-methoxycarbonylbenzyltriphenylphosphonium bromide (1.17 g) in THF (8 ml), potassium t-butoxide (246 mg) was added in a stream of argon. The mixture was stirred for 30 minutes. A solution of 2-nitro-5-chlorobenzoic acid chloride (prepared in Reference Example 13.) in THF (4 ml) was added dropwise to the reaction solution. The mixture was stirred for 3 hours at room temperature. The reaction mixture was quenched by adding saturated aqueous ammonium chloride and extracted with chloroform. The organic layer was washed, dried over and concentrated under the reduced pressure. The residue was purified on silica gel column chromatography ($CHCl_3$-MeOH) to give the title compound (619 mg) having the following physical data.

TLC : Rf 0.26 ($CHCl_3$: MeOH = 100 : 1).

Reference Example 15

Methyl 4-[2-(2-nitro-5-chlorophenyl)ethynyl]benzoate

[0187]



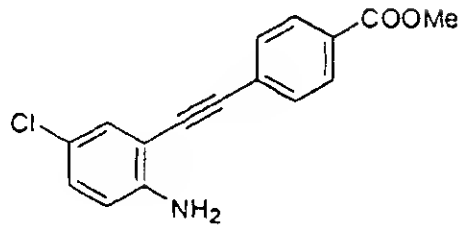
[0188] A solution of 1-(2-nitro-5-chlorobenzoyl)-1-(4-methoxycarbonylphenyl)methylidene triphenylphosphoran (513 mg; prepared in Reference Example 14.) in o-dichlorobenzene (10 ml) was refluxed for 9 hours at 180°C in a stream of argon. The reaction mixture was concentrated under the reduced pressure. The residue was purified on silica gel column chromatography (hexane-AcOEt) to give the title compound (189 mg) having the following physical data.

TLC : Rf 0.39 (hexane : AcOEt = 7 : 1).

Reference Example 16

Methyl 4-[2-(2-amino-5-chlorophenyl)ethynyl]benzoate

[0189]

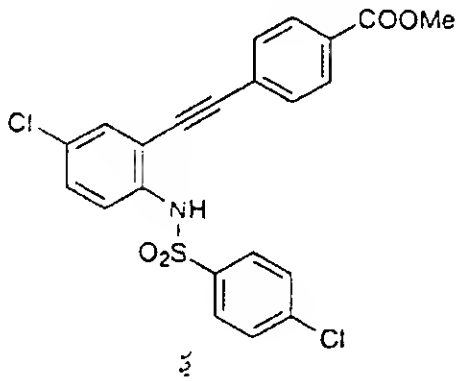


[0190] To a solution of methyl 4-[2-(2-nitro-5-chlorophenyl)ethynyl]benzoate (180 mg; prepared in Reference Example 15.) in acetic acid (3.6 ml), reduced iron powder (160 mg) was added. The mixture was refluxed for 30 minutes and filtered. The filtrate was concentrated under the reduced pressure. The residue was purified on silica gel column chromatography (hexane-AcOEt) to give the title compound (144 mg) having the following physical deta. TLC : Rf 0.25 (hexane : AcOEt = 5 . 1).

Example 13

Methyl 4-[2-[2-(4-chlorophenylsulfonylamino)-5-chlorophenyl]ethynyl]benzoate

[0191]



[0192] To a solution of methyl 4-[2-(2-amino-5-chlorophenyl)ethynyl]benzoate (136 mg; prepared in Reference Example 16.) in methylene chloride (2 ml), pyridine (77 µl) and 4-chlorobenzenesulfonyl chloride (106 mg) were added at 0°C under an atmosphere of argon. The mixture was stirred for 24 hours at room temperature. The reaction mixture was diluted with ethyl acetate, washed, dried over and concentrated under the reduced pressure. The residue was purified on silica gel column chromatography (hexane-AcOEt) to give the title compound (207 mg) having the following physical date.

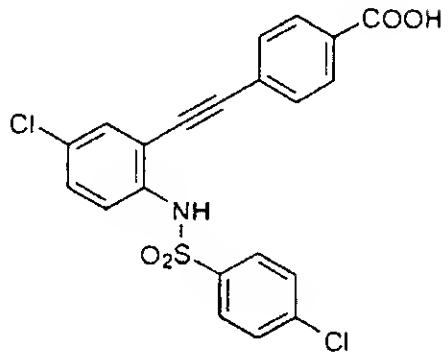
TLC : Rf 0.50 (hexane : AcOEt = 3 : 1);
NMR : δ 8.07 (2H, d), 7.67 (2H, d), 7.58 (1H, d), 7.49 (2H, d), 7.39 (1H, d), 7.34 (2H, d), 7.32 (1H, dd), 7.07 (1H,

brs), 3.96 (3H, s).

Example 14

4-[2-[2-(4-chlorophenylsulfonylamino)-5-chlorophenyl]ethynyl]benzoic acid

[0193]



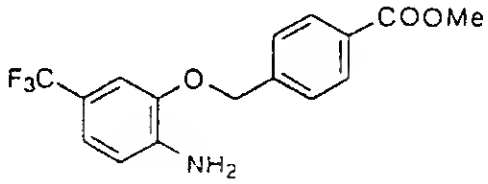
[0194] By using methyl 4-[2-[2-(4-chlorophenylsulfonylamino)-5-chlorophenyl]ethynyl]benzoate (199 mg; prepared in Example 13.), the title compound (181 mg) having the following physical data was obtained by the same procedure as Example 2.

TLC : Rf 0.43 ($CHCl_3$: MeOH : AcOH= 100 : 5 : 1);
NMR (DMSO-d_6) : δ 13.16 (1H, brs), 10.32 (1H, brs), 8.00 (2H, d), 7.65 (2H, d), 7.59 (1H, d), 7.57 (2H, d), 7.50 (1H, dd), 7.43 (2H, d), 7.35 (1H, d).

Reference Example 17

Methyl 4-(2-amino-5-trifluoromethylphenoxymethyl)benzoate

[0195]



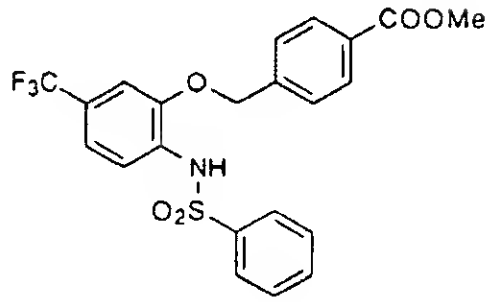
[0196] By using 2-nitro-5-trifluoromethylphenol, the title compound having the following physical data was obtained by the same procedure as Reference Example 6→ Reference Example 12.

TLC : Rf 0.33 (hexane : AcOEt = 3 : 1).

Example 15

Methyl 4-(2-phenylsulfonylamino-5-trifluoromethylphenoxymethyl)benzoate

[0197]



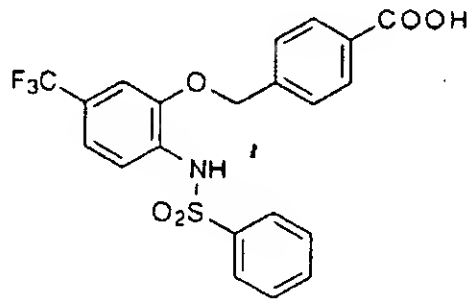
[0198] By using methyl 4-(2-amino-5-trifluoromethylphenoxymethyl)benzoate (prepared in Reference Example 17.), the title compound having the following physical deta was obtained by the same procedure es Example 7.

TLC : Rf 0.76 (benzene : acetone = 9 : 1);
NMR : δ 8.05 (2H, d, J=8.2Hz), 7.77 (2H, m), 7.69 (1H, d, J=8.6Hz),7.58 (1H, m), 7.45 (2H, m), 7.25 (3H, m), 7.18 (1H, m), 6.99 (1H, m), 5.02 (2H, s), 3.95 (3H, s).

Example 16

4-(2-phenylsulfonylamino-5-trifluoromethylphenoxymethyl)benzoic acid

[0199]



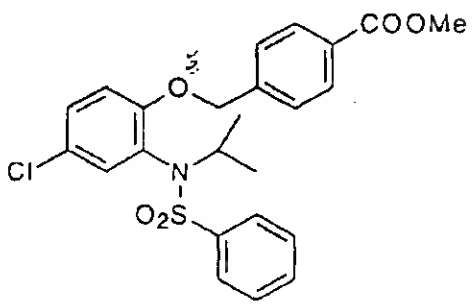
[0200] By using methyl 4-(2-phenylsulfonylamino-5-trifluoromethylphenoxymethyl)benzoate (prepared in Example 15.), the title compound having the following physical date was obtained by the same procedure as Exemple 2.

TLC : Rf 0.52 ($CHCl_3$: MeOH : AcOH= 100 : 5 : 1);
NMR (DMSO-d_6) : δ 12.95 (1H, brd), 10.10 (1H, brd), 7.93 (2H, d, J=8.0Hz), 7.75 (2H, m), 7.59 (1H, m), 7.40-7.53 (5H, m), 7.27 (2H, m), 5.14 (2H, s).

Example 17

Methyl 4-[2-(N-isopropyl-phenylsulfonylamino)-4-chlorophenoxymethyl]benzoate

[0201]



[0202] To a solution of methyl 4-(2-phenylsulfonylamino-4-chlorophenoxymethyl)benzoate (402 mg; prepared in Example 7(e).) in DMF (4 ml), potassium carbonate (256 mg) and isopropyl iodide (185 ml) were added. The mixture was stirred overnight at room temperature and for 9 hours at 50°C. To the reaction solution, iced water and 2N HCl were added. The mixture was extracted with ethyl acetate. The organic layer was washed, dried over, concentrated after filtration, solidified with ethanol and washed to give the title compound (411 mg) having the following physical data.

TLC : Rf 0.59 (hexane . AcOEt = 2 : 1);
NMR : δ 8.05 (2H, d, J=8.8Hz), 7.83-7.79 (2H, m), 7.55-7.26 (6H, m), 7.08 (1H, d, J=2.8Hz), 6.89 (1H, d, J=8.8Hz), 5.04 (2H, s), 4.36 (1H, sept, J=6.8Hz), 3.93 (3H, s), 1.05 (6H, d, J=6.8Hz).

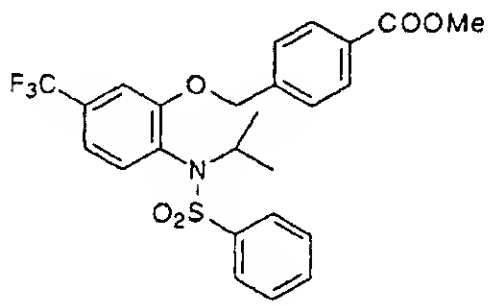
Example 17(1)-(4)

[0203] By using the corresponding compounds, the title compounds having the following physicel data were obtained by the same procedure as Reference Example 6→Reference Example 7→Example 7→Example 17 or Reference Example 8→Reterence Example 9→Reference Example 10→Example 9→Example 17.

Example 17(1)

Methyl 4-[2-(N-isopropyl-phenylsulfonylamino)-5-trifluoromethylphenoxymethyl]benzoat

[0204]

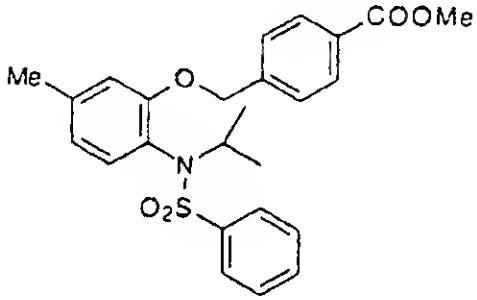


TLC : Rf 0.55 (hexane : AcOEt = 2 : 1);
NMR : δ 8.07 (2H, d, J=8.4Hz), 7.79 (2H, m), 7.44-7.55 (3H, m), 7.32-7.43 (2H, m), 7.18-7.29 (3H, m), 5.10 (2H, s), 4.38 (1H, sept, J=6.6Hz), 3.94 (3H, s), 1.05 (6H, d, J=6.6Hz).

Example 17(2)

Methyl 4-[2-(N-isopropyl-phenylsulfonylamino)-5-methylphenoxymethyl]benzoate

[0205]

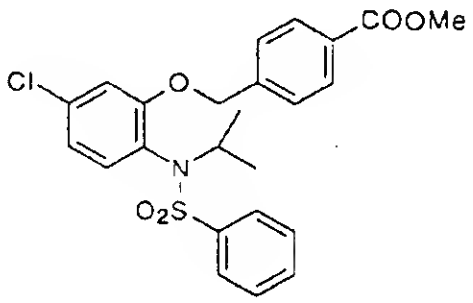


TLC : Rf 0.48 (hexane : AcOEt = 2 : 1);
NMR : δ 8.04 (2H, d, J=8.4Hz), 7.80 (2H, m), 7.41-7.52 (3H, m), 7.28-7.39 (2H, m), 6.97 (1H, d, J=8.6Hz), 6.73-6.80 (2H, m), 5.00 (2H, s), 4.38 (1H, sept, J=7.0Hz), 3.93 (3H, s), 2.35 (3H, s), 1.05 (6H, d, J=7.0Hz).

Example 17(3)

Methyl 4-[2-(N-isopropyl-phenylsulfonylamino)-5-chlorophenoxymethyl]b nzoate

[0206]

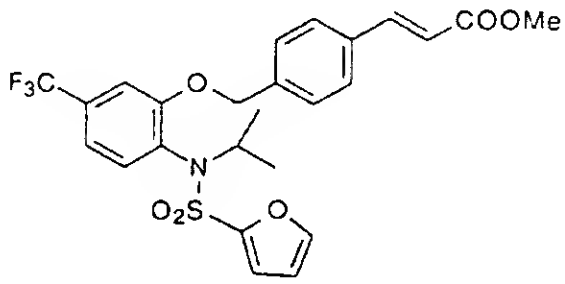


TLC : Rf 0.30 (hexane : AcOEt = 4 : 1);
NMR : δ 8.06 (2H, d, J=8.2Hz), 7.78 (2H, d, J=7.2Hz), 7.25-7.48 (5H, m), 6.85-7.05 (3H, m), 5.02 (2H, s), 4.37 (1H, sept, J=6.4Hz), 3.94 (3H, s), 1.04 (6H, d, J=6.4Hz).

Example 17(4)

Methyl 4-[2-(N-isopropyl-2-furanylsulfonylamino)-5-trifluoromethylphenoxymethyl]cinnamate

[0207]

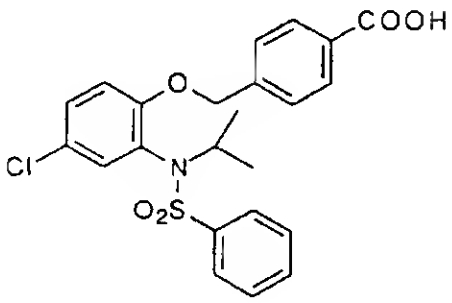


TLC : Rf 0.39 (benzene : AcOEt = 19 : 1);
NMR : δ 7.71 (1H, d, J=16Hz), 7.59-7.45 (5H, m), 7.23-7.20 (3H, m), 6.94-6.92 (1H, m), 6.50-6.42 (2H, m), 5.12 (2H, s), 4 5-4.4 (1H, m), 3.82 (3H, s), 1.09 (6H, dd, J=6.5, 2Hz)

Example 18

4-[2-(N-isopropyl-phenylsulfonylamino-4-chlorophenoxymethyl]benzoic acid

[0208]



[0209] By using methyl 4-[2-(N-isopropyl-phenylsulfonylamino)-4-chlorophenoxymethyl]benzoate (prepared in Example 17.), the title compound having the following physical data was obtained by the same procedure as Example 2.

TLC : Rf 0.43 ($CHCl_3$: MeOH : H_2O = 9 : 1 : 0.1);
NMR (DMSO-d_6) : δ 12.90 (1H, br), 7.94 (2H, d, J=8.4Hz), 7.78 (2H, d, J=8.4Hz), 7.66-7.45 (6H, m), 7.23 (1H, d, J=8.4Hz), 7.07 (1H, d, J=2.4Hz), 5.13 (2H, s), 4.20 (1H, sept, J=6.6Hz), 0.99 and 0.96 (each 3H, each d, J=6.6Hz).

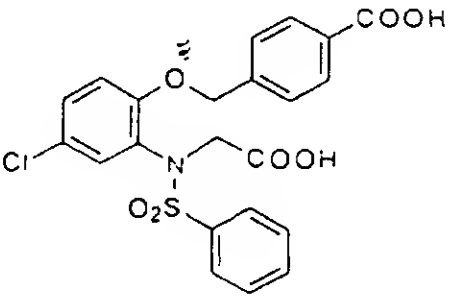
Example 18(1)-18(128)

[0210] By using the corresponding compounds, the title compounds having the following physical data were obtained by the same procedure as Reference Example 6→Reference Example 7→Example 7→Example 17→Example 2 or Reference Example 8→Reference Example 9→Reference Example 10→Example 9→Example 17→Example 2.

Example 18(1)

4-[2-(N-carboxymethyl-phenylsulfonylamino)-4-chlorophenoxymethyl]benzoic acid

[0211]

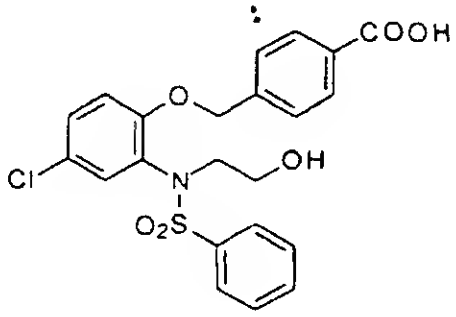


TLC : Rf 0.20 ($CHCl_3$: MeOH : H_2O = 7 : 3 : 0.3);
NMR (DMSO-d_6) : δ 12.93 (2H, br), 7.88 (2H, d, J=8.4Hz), 7.63-7.37 (7H, m), 7.16-7.06 (3H, m), 4.88 (2H, s), 4.31 (2H, s).

Example 18(2)

4-[2-[N-(2-hydroxyethyl)-phenylsulfonylamino]-4-chlorophenoxymethyl]benzoic acid

[0212]

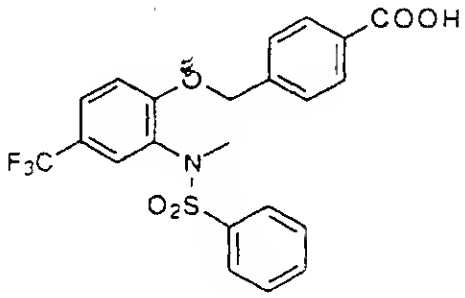


TLC : Rf 0.26 ($CHCl_3$: MeOH : H_2O = 9 : 1 : 0.1);
NMR (DMSO-d_6) : δ 12.71 (1H, br), 7.88 (2H, d, J=8.4Hz), 7.63-7.32 (7H, m), 7.19-7.08 (3H, m), 4.89 (2H, brs), 4.71 (1H, br), 3.86-3.40 (4H, m).

Example 18(3)

4-[2-(N-methyl-phenylsulfonylamino)-4-trifluoromethylphenoxymethyl]benzoic acid

[0213]

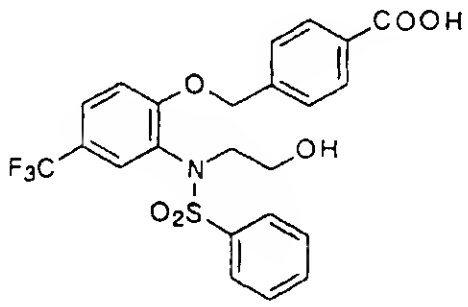


TLC : Rf 0.31 ($CHCl_3$: MeOH : H_2O = 9 . 1 0.1);
NMR (DMSO-d_6) . δ 12.90 (1H, br), 7.90 (2H, d, J=8.4Hz), 7.76-7.70 (1H, dd-like), 7.64-7.43 (6H, m), 7.31 (1H, d, J=8.4Hz), 7.23 (2H, d, J=8.4Hz), 5.05 (2H, s), 3.18 (3H, s).

Example 18(4)

4-[2-[N-(2-hydroxyethyl)-phenylsulfonylamino]-4-trifluoromethylphenoxymethyl]benzoic acid

[0214]

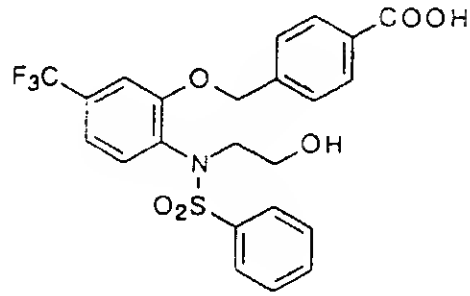


TLC: Rf 0.24 ($CHCl_3$: MeOH : H_2O = 9 : 1 : 0.1);
NMR (DMSO-d_6) : δ 12.51 (1H, br), 7.89 (2H, d, J=8.4Hz), 7.74 (1H, dd, J=2.2 and 8.4Hz), 7.62-7.37 (6H, m), 7.28 (1H, d, J=8.4Hz), 7.20 (2H, d, J=8.4Hz), 5.00 (2H, brs), 4.70 (1H, br), 3.66-3.28 (4H, m).

Example 18(5)

4-[2-[N-(2-hydroxyethyl)-phenylsulfonylamino]-5-trifluoromethylphenoxymethyl]benzoic acid

[0215]

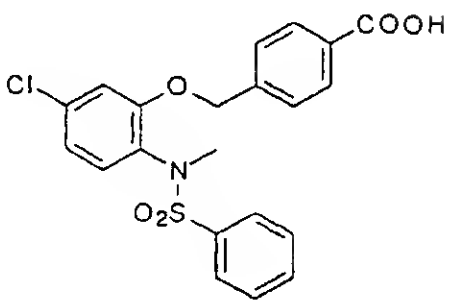


TLC : Rf 0.40 ($CHCl_3$: MeOH : AcOH= 100 : 5 : 1);
NMR (DMSO-d_6) : δ 12.96 (1H, brd), 7.89 (2H, d, J=8.4Hz), 7.61 (2H, m), 7.34-7.58 (6H, m), 7.20 (2H, d, J=8.4Hz), 5.05 (1H, brs), 4.67 (1H, m), 3.60 (2H, m), 3.42 (2H, m).

Example 18(6)

4-[2-(N-methyl-phenylsulfonylamino)-5-chlorophenoxym thyl]benzoic acid

[0216]

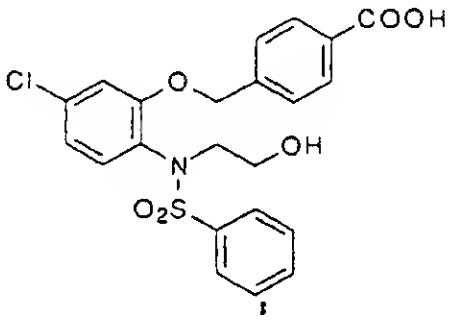


TLC : Rf 0.36 ($CHCl_3$: MeOH : H_2O = 9 : 1 : 0.1);
NMR (DMSO-d_6) : δ 12.63 (1H, br), 7.89 (2H, d, J=8.4Hz), 7.64-7.41 (5H, m), 7.25-7.19 (4H, m), 7.05 (1H, dd, J=2.2 and 8.4Hz), 4.98 (2H, s), 3.12 (3H, s).

Example 18(7)

4-[2-[N-(2-hydroxyethyl)-phenylsulfonylamino]-5-chlorophenoxymethyl]benzoic acid

[0217]

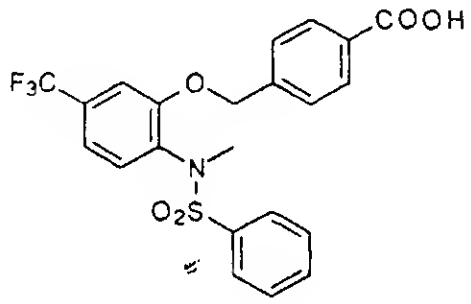


TLC : Rf 0.27 ($CHCl_3$: MeOH : H_2O = 9 : 1 : 0.1);
NMR (DMSO-d_6) : δ 12.88 (1H, br), 7.89 (2H, d, J=8.4Hz), 7.62-7.36 (5H, m), 7.29-7.17 (4H, m), 7.06 (1H, dd, J=2.2 and 8.4Hz), 4.95 (2H, brs), 4.68 (1H, br), 3.66-3.24 (4H, br).

Example 18(8)

4-[2-(N-methyl-phenylsulfonylamino)-5-trifluoromethylph noxymethyl]benzoic acid

[0218]

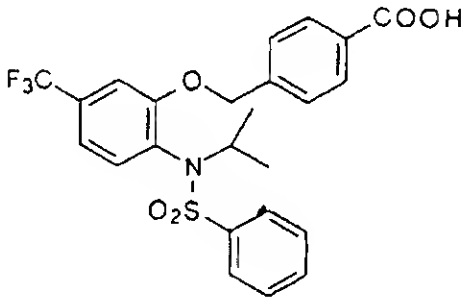


TLC : Rf 0.46 ($CHCl_3$: MeOH : AcOH= 100 : 5 : 1);
NMR : δ 8.08 (2H, d, J=8.0Hz), 7.68 (2H, m), 7.12-7.53 (8H, m), 4.93 (2H, s), 3.24 (3H, s).

Example 18(9)

4-[2-(N-isopropyl-phenylsulfonylamino)-5-trifluoromethylphenoxymethyl]benzoic acid

[0219]

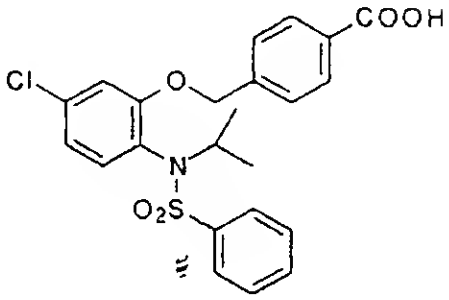


TLC : Rf 0.44 ($CHCl_3$: MeOH : AcOH= 100 : 5 : 1);
NMR : δ 8.15 (2H, d, J=8.6Hz), 7.81 (2H, m), 7.52 (3H, m), 7.38 (2H, m), 7.24 (3H, m), 5.13 (2H, s), 4.40 (1H, sept, J=6 8Hz), 1.06 (6H, d, J=6.8Hz)

Example 18(10)

4-[2-(N-isopropyl-phenylsulfonylamino)-5-chlorophenoxymethyl]benzoic acid

[0220]

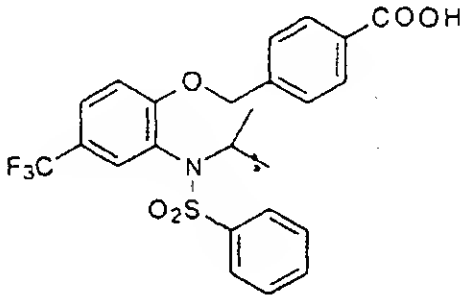


TLC : Rf 0.35 ($CHCl_3$: MeOH : H_2O = 9 : 1 : 0.1);
NMR (DMSO-d_6) : δ 12.96 (1H, br), 7.95 (2H, d, J=8.2Hz), 7.78-7.74 (2H, m), 7.65-7.43 (5H, m), 7.32 (1H, s), 7.07 (2H, s), 5.21 and 5.07 (each 1H, each d, J=15.6Hz), 4.21 (1H, sept-like), 0.94 (6H, d, J=6.8Hz).

Example 18(11)

4-[2-(N-isopropyl-phenylsulfonylamino)-4-trifluoromethylphenoxymethyl]benzoic acid

[0221]

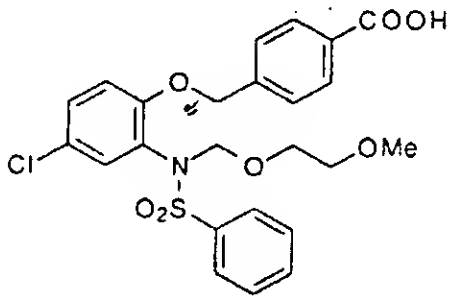


TLC : Rf 0.30 ($CHCl_3$: MeOH : H_2O = 9 . 1 . 0.1);
NMR (DMSO-d_6) : δ 13.03 (1H, br), 7.95 (2H, d, J=8.2Hz), 7.84-7.74 (3H, m), 7.67-7.39 (6H, m), 7.25 (1H, d, J=2.4Hz), 5.28 and 5.21 (each 1H, each d, J=16.6Hz), 4.26 (1H, sept-like), 0.98 and 0.97 (each 3H, each d, J=6.6Hz)

Example 18(12)

4-[2-[N-(2-methoxyethoxymethyl)-phenylsulfonylamino]-4-chlorophenoxymethyl]benzoic acid

[0222]

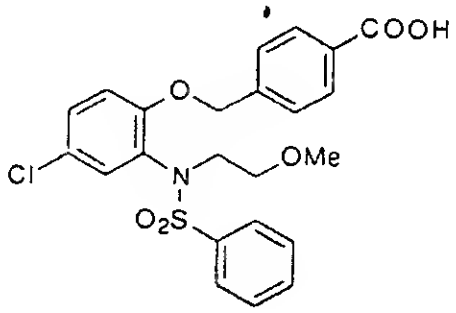


TLC : Rf 0.40 ($CHCl_3$: MeOH : H_2O = 9 : 1 : 0.1);
NMR ($DMSO-d_6$) : δ 12.98 (1H, br), 7.91 (2H, d, J=8.2Hz), 7.66-7.52 (3H, m), 7.45-7.38 (3H, m), 7.26-7.22 (3H, m), 7.10 (1H, d, J=8.2Hz), 5.06 (2H, brs), 4.92 (2H, brs), 3.68-3.63 (2H, t-like), 3.42-3.37 (2H, t-like), 3.21 (3H, s).

Example 18(13)

4-[2-[N-(2-methoxyethyl)-phenylsulfonylamino]-4-chlorophenoxymethyl]benzoic acid

[0223]

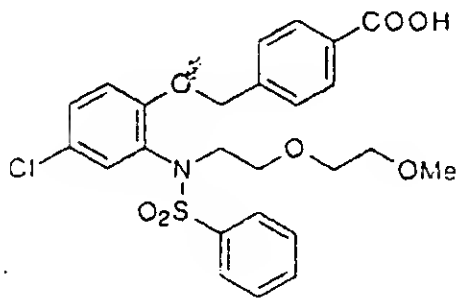


TLC : Rf 0.25 ($CHCl_3$: MeOH : H_2O = 9 : 1 : 0.1);
NMR ($DMSO-d_6$) : δ 12.92 (1H, br), 7.88 (2H, d, J=8.2Hz), 7.64-7.39 (6H, m), 7.22-7.10 (4H, m), 4.91 (2H, brs), 3.69 (2H, br), 3.38-3.33 (2H, m), 3.13 (3H, s)

Example 18(14)

4-[2-[N-[2-(2-methoxyethoxy)ethyl]-phenylsulfonylamino]-4-chlorophenoxymethyl]benzoic acid

[0224]

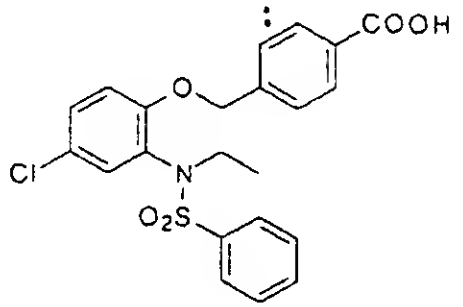


TLC : Rf 0.29 ($CHCl_3$: MeOH : H_2O = 9 : 1 : 0.1);
NMR ($DMSO-d_6$) : δ 12.95 (1H, br), 7.89 (2H, d, J=8.2Hz), 7.65-7.39 (6H, m), 7.25 (1H, d, J=2.6Hz), 7.20 (2H, d, J=8.2Hz), 7.11 (1H, d, J=8.2Hz), 4.92 (2H, brs), 3.69 (2H, br), 3.47-3.28 (6H, m), 3.19 (3H, s).

Example 18(15)

4-[2-(N-ethyl-phenylsulfonylamino)-4-chlorophenoxymethyl]benzoic acid

[0225]

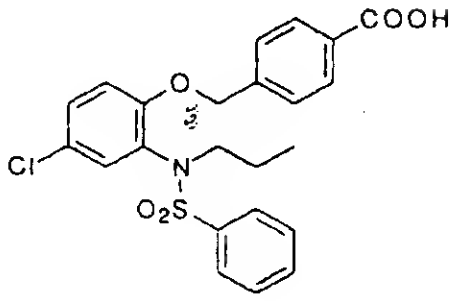


TLC : Rf 0.51 ($CHCl_3$: MeOH = 9 : 1);
NMR : δ 8.08 (2H, d, J=8.2Hz), 7.8-7.6 (2H, m), 7.5-7.2 (7H, m), 6.81 (1H, d, J=9.4Hz), 4.88 (2H, s), 3.67 (2H, q, J=7.0Hz), 1.11 (3H, t, J=7.0Hz).

Example 18(16)

4-[2-(N-propyl-phenylsulfonylamino)-4-chlorophenoxymethyl]benzoic acid

[0226]

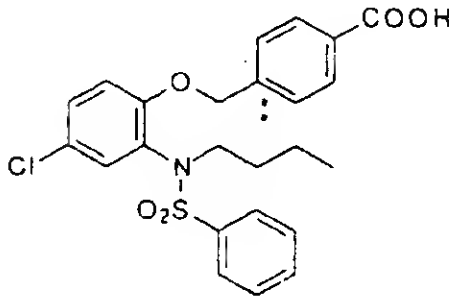


TLC : Rf 0.50 ($CHCl_3$: MeOH = 9 : 1);
NMR : δ 8.08 (2H, d, J=8.4Hz), 7.7-7.6 (2H, m), 7.5-7.2 (7H, m), 6.80 (1H, d, J=9.6Hz), 4.85 (2H, s), 3.6-3.5 (2H, m), 1.6-1.4 (2H, m), 0.89 (3H, t, J=7.2Hz).

Example 18(17)

4-[2-(N-butyl-phenylsulfonylamino)-4-chlorophenoxymethyl]benzoic acid

[0227]

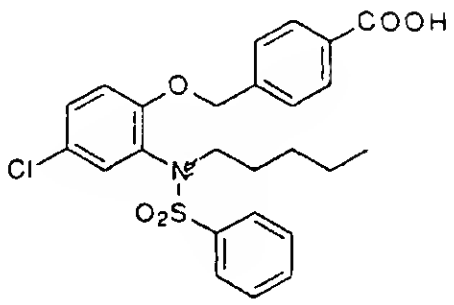


TLC : Rf 0.53 ($CHCl_3$: MeOH = 9 : 1);
NMR : δ 8.08 (2H, d, J=8.4Hz), 7.7-7.6 (2H, m), 7.5-7.2 (7H, m), 6.80 (1H, d, J=9.4Hz), 4.86 (2H, s), 3.7-3.5 (2H, m), 1.5-1.2 (4H, m), 0.85 (3H, t, J=7.0Hz).

Example 18(18)

4-[2-(N-pentyl-phenylsulfonylamino)-4-chlorophenoxymethyl]benzoic acid

[0228]

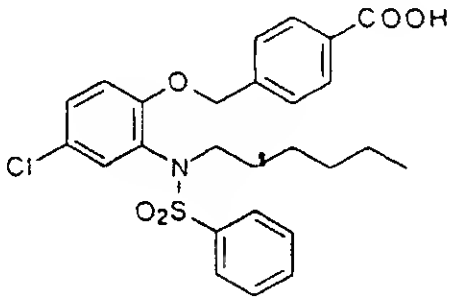


TLC : Rf 0.56 ($CHCl_3$: MeOH = 9 : 1);
NMR : δ 8.08 (2H, d, J=8.2Hz), 7.7-7.6 (2H, m), 7.5-7.2 (7H, m), 6.8-6.7 (1H, m), 4.86 (2H, s), 3.6-3.5 (2H, m), 1.5-1.2 (6H, m), 0.9-0.8 (3H, m).

Example 18(19)

4-[2-(N-hexyl-phenylsulfonylamino)-4-chlorophenoxymethyl]benzoic acid

[0229]

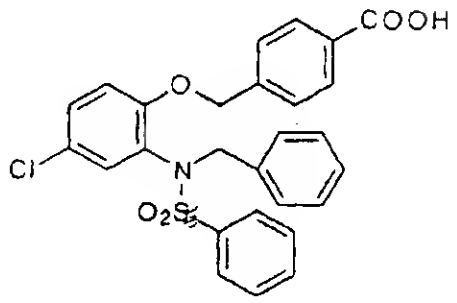


TLC : Rf 0.58 ($CHCl_3$: MeOH = 9 . 1);
NMR : δ 8 08 (2H, d, J=8.6Hz), 7.7-7.6 (2H, m), 7.5-7.2 (7H, m), 6.9-6.8 (1H, m), 4.86 (2H, s), 3.6-3.5 (2H, m), 1.5-1.1 (8H, m), 0.9-0.8 (3H, m).

Example 18(20)

4-[2-(N-benzyl-ph nylsulfonylamino)-4-chlorophenoxymethyl]benzoic acid

[0230]

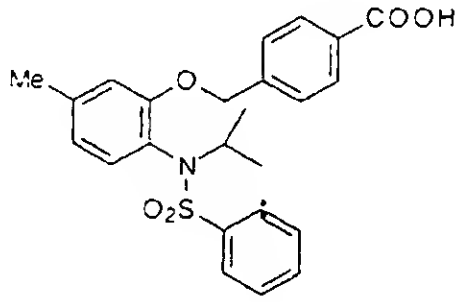


TLC : Rf 0.60 ($CHCl_3$: MeOH = 9 : 1);
NMR : δ 8.09 (2H, d, J=8.6Hz), 7.8-7.7 (2H, m), 7.6-7.3 (3H, m), 7.3-7.1 (9H, m), 6.71 (1H, d, J=8.8Hz), 4.82 (2H, s), 4.78 (2H, s).

Example 18(21)

4-[2-(N-isopropyl-phenylsulfonylamino)-5-methylphenoxymethyl]benzoic acid

[0231]

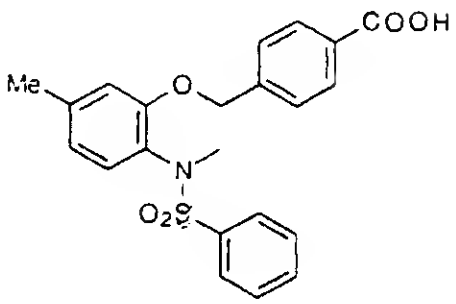


TLC : Rf 0.50 ($CHCl_3$: MeOH : AcOH= 100 : 5 : 1);
NMR : δ 8.13 (2H, d, J=8.2Hz), 7.82 (2H, m), 7.49 (3H, m), 7.36 (2H, m), 6.98 (1H, d, J=8.6Hz), 6.77 (2H, m), 5.05 (2H, s), 4.40 (1H, sept, J=6.6Hz), 2.36 (3H, s), 1.05 (6H, d, J=6.6Hz).

Example 18(22)

4-[2-(N-methyl-phenylsulfonylamino)-5-methylphenoxymethyl]benzoic acid

[0232]

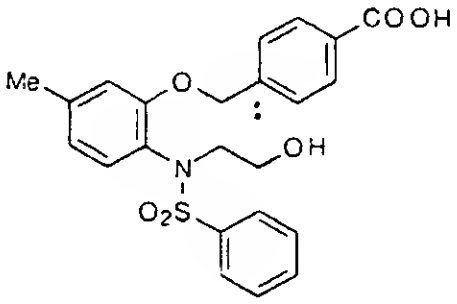


TLC : Rf 0.56 (AcOEt : hexane : AcOH= 9 : 10 : 1);
NMR (DMSO-d_6) : δ 12.96 (1H, brs), 7.89 (2H, d, J=8.5Hz), 7.67-7.40 (5H, m), 7.23 (2H, d, J=8.0Hz), 7.06 (1H, d, J=8.0Hz), 6.93 (1H, s), 6.78 (1H, d, J=8.0Hz), 4.93 (2H, s), 3.12 (3H, s), 2.30 (3H, s).

Example 18(23)

4-[2-[N-(2-hydroxyethyl)-phenylsulfonylamino]-5-methylphenoxymethyl]benzoic acid

[0233]

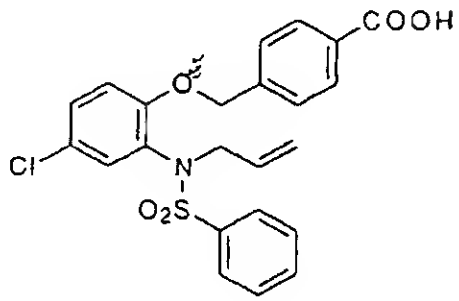


TLC : Rf 0.27 (AcOEt : hexane : AcOH= 9 . 10 : 1);
NMR (DMSO-d_6) : δ 12.95 (1H, brs), 7.87 (2H, d, J=8.5Hz), 7.55-7.32 (5H, m), 7.20 (2H, d, J=8.5Hz), 7.08 (1H, d, J=8.0Hz), 6.91 (1H, s), 6.77 (1H, d, J=8.0Hz), 4.89 (2H, brs), 4.63 (1H, t, J=4.0Hz), 3.50-3.20 (4H, m), 2.29 (3H, s).

Example 18(24)

4-[2-[N-(prop-2-enyl)-phenylsulfonylamino]-4-chlorophenoxymethyl]benzoic acid

[0234]

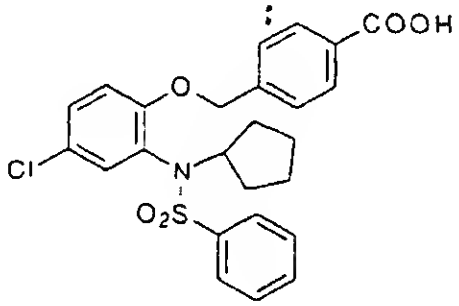


TLC : Rf 0.54 ($CHCl_3$: MeOH = 9 : 1);
NMR : δ 8.08 (2H, d, J=8.0Hz), 7.8-7.6 (2H, m), 7.6-7.2 (7H, m), 6.78 (1H, d, J=9.4Hz), 5.9-5.6 (1H, m), 5.2-5.0 (2H, m), 4.86 (2H, s), 4.3-4.2 (2H, m).

Example 18(25)

4-[2-(N-cyclopentyl-phenylsulfonylamino)-4-chlorophenoxymethyl]benzoic acid

[0235]

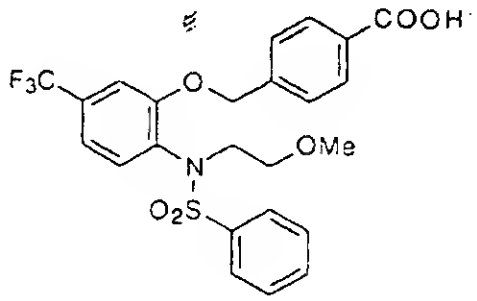


TLC : Rf 0.47 ($CHCl_3$: MeOH = 9 : 1);
NMR : δ 8.13 (2H, d, J=8.4Hz), 7.9-7.8 (2H, m), 7.6-7.2 (6H, m), 7.07 (1H, d, J=2.6Hz), 6.88 (1H, d, J=8.8Hz), 5.1-5.0 (2H, m), 4.5-4.3 (1H, m), 2.0-1.7 (2H, m), 1.6-1.2 (6H, m).

Example 18(26)

4-[2-[N-(2-methoxyethyl)-phenylsulfonylamino]-5-trifluoromethylphenoxymethyl]benzoic acid

[0236]

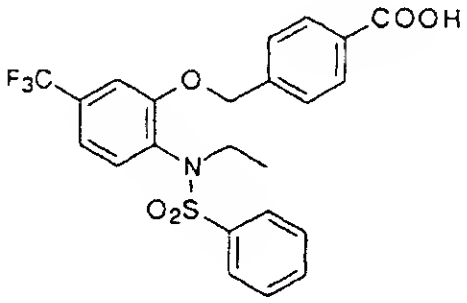


TLC : Rf 0.46 ($CHCl_3$: MeOH : AcOH= 100 : 5 : 1);
NMR : δ 8.07 (2H, d, J=8.4Hz), 7.66 (2H, m), 7.18-7.53 (7H, m), 7.12 (1H, m), 4.90 (2H, s), 3.81 (2H, m), 3.51 (2H, t, J=6.0Hz), 3.24 (3H, s).

Example 18(27)

4-[2-(N-ethyl-phenylsulfonylamino)-5-trifluoromethylphenoxymethyl]benzoic acid

[0237]

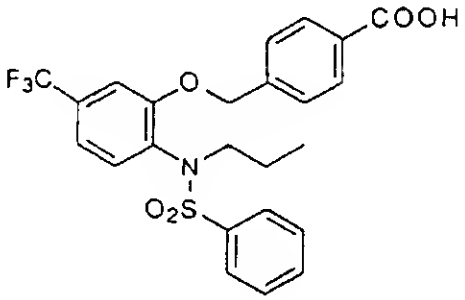


TLC : Rf 0.43 ($CHCl_3$: MeOH = 9 : 1);
NMR : δ 8.09 (2H, d, J=8.4Hz), 7.7-7.6 (2H, m), 7.5-7.2 (7H, m), 7.15 (1H, d, J=1.6Hz), 4.94 (2H, s), 3.69 (2H, q, J=7.4Hz), 1.11 (3H, t, J=7.4Hz).

Example 18(28)

4-[2-(N-propyl-phenylsulfonylamino)-5-trifluoromethylphenoxymethyl]benzoic acid

[0238]

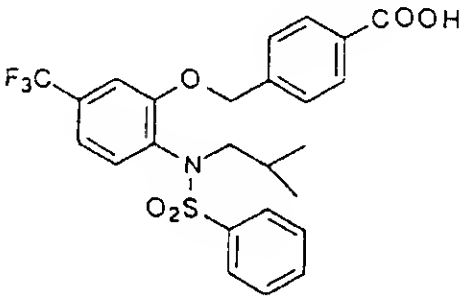


TLC : Rf 0.5 ($CHCl_3$: MeOH = 9 : 1);
NMR : δ 8.09 (2H, d, J=8.2Hz), 7.7-7.6 (2H, m), 7.5-7.2 (7H, m), 7.14 (1H, s), 4.92 (2H, s), 3.59 (2H, t, J=7.4Hz), 1.6-1.4 (2H, m), 0.88 (3H, t, J=7.4Hz).

Example 18(29)

4-[2-(N-isobutyl-phenylsulfonylamino)-5-trifluoromethylphenoxymethyl]benzoic acid

[0239]

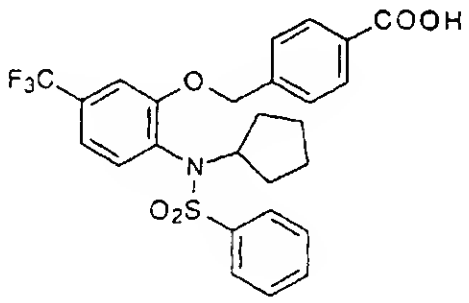


TLC : Rf 0.53 ($CHCl_3$: MeOH = 9 : 1).
NMR : δ 8.10 (2H, d, J=8.4Hz), 7.7-7.6 (2H, m), 7.5-7.2 (7H, m), 7.11 (1H, d, J=1.6Hz), 5.0-4.8 (2H, m), 3.44 (2H, d, J=7.4Hz), 1.7-1.5 (1H, m), 0.90 (6H, d, J=6.4Hz).

Example 18(30)

4-[2-(N-cyclopentyl-phenylsulfonyamino)-5-trifluoromethylphenoxymethyl]benzoic acid

[0240]

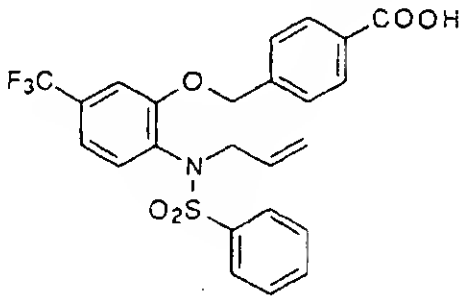


TLC : Rf 0.54 ($CHCl_3$: MeOH = 9 : 1);
NMR : δ 8.15 (2H, d, J=8.0Hz), 7.8-7.7 (2H, m), 7.6-7.3 (5H, m), 7.3-7.2 (3H, m), 5.2-5.0 (2H, m), 4.5-4.3 (1H, m), 2.0-1.8 (2H, m), 1.6-1.2 (6H, m).

Example 18(31)

4-[2-[N-(prop-2-enyl)-phenylsulfonylamino]-5-trifluoromethylphenoxymethyl]benzoic acid

[0241]

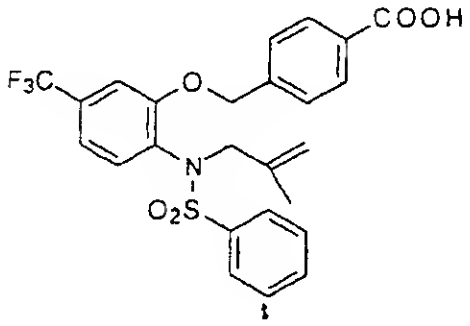


TLC : Rf 0.47 ($CHCl_3$: MeOH = 9 : 1);
NMR : δ 8 10 (2H, d, J=8.6Hz), 7.8-7.6 (2H, m), 7 6-7.2 (7H, m), 7 12 (1H, s), 5.9-5.6 (1H, m), 5.1-5.0 (2H, m), 4.93 (2H, s), 4.24 (2H, d, J=6.2Hz).

Example 18(32)

4-[2-[N-(2-methylprop-2-enyl)-phenylsulfonylamino]-5-trifluoromethylphenoxymethyl]benzoic acid

[0242]

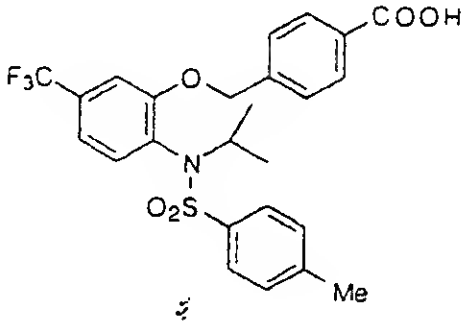


TLC : Rf 0.48 ($CHCl_3$: MeOH = 9 : 1);
NMR : δ 8.10 (2H, d, J=8.4Hz), 7.7-7.6 (2H, m), 7.5-7.2 (7H, m), 7.10 (1H, s), 4.89 (2H, s), 4.71 (2H, d, J=12.0Hz), 4.20 (2H, s), 1.74 (3H, s).

Example 18(33)

4-[2-(N-isopropyl-4-methylphenylsulfonylamino)-5-trifluoromethylphenoxymethyl]benzoic acid

[0243]

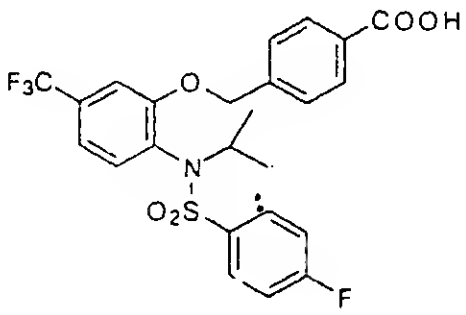


TLC : Rf 0.60 ($CHCl_3$: MeOH : AcOH= 100 : 5 : 1);
NMR : δ 8.14 (2H, d, J=8.4Hz), 7.68 (2H, d, J=8.2Hz), 7.52 (2H, d, J=8.2Hz), 7.19 (5H, m, arom), 5.14 (2H, s), 4.38 (1H, sept., J=6.8Hz), 2 38 (3H, s), 1.05 (6H, d, J=6.8Hz).

Example 18(34)

4-[2-(N-isopropyl-4-fluorophenylsulfonylamino)-5-trifluoromethylphenoxymethyl]benzoic acid

[0244]

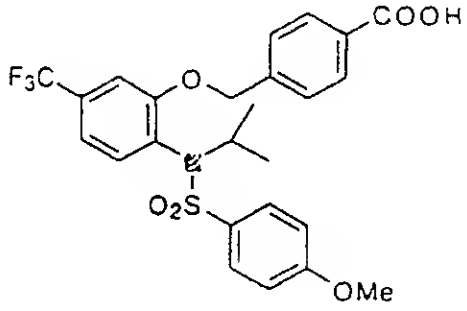


TLC : Rf 0.60 ($CHCl_3$: MeOH : AcOH= 100 : 5 : 1),
NMR : δ 8.16 (2H, d, J=8.2Hz), 7.76 (2H, m, arom), 7.52 (2H, d, J=8.2Hz), 7.26 (3H, m, arom), 7.01 (2H, m, arom), 5.10 (2H, dd, J=11.8, 14.6Hz), 4.38 (1H, sept., J=6.4Hz), 1.09 (3H, d, J=6.4Hz), 1.07 (3H, d J=6.4Hz).

Example 18(35)

4-[2-(N-isopropyl-4-methoxyphenylsulfonylamino)-5-trifluoromethylphenoxymethyl]benzoic acid

[0245]

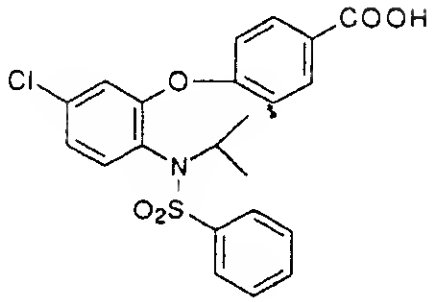


TLC : Rt 0.60 ($CHCl_3$: MeOH : AcOH= 100 : 5 : 1),
NMR . δ 8.15 (2H, d, J=8.2Hz), 7.72 (2H, d, J=8.8Hz), 7.53 (2H, d, J=8.2Hz), 7.18 (3H, m, arom), 6.81 (2H, d, J=9.2Hz), 5.14 (2H, s), 4.35 (1H, sept., J=6.4Hz), 3.83 (3H, s), 1.08 (3H, d, J=6.4Hz), 1 05 (3H, d, J=6.4Hz).

Example 18(36)

4-[2-(N-isopropyl-phenylsulfonylamino)-5-chlorophenoxy]benzoic acid

[0246]

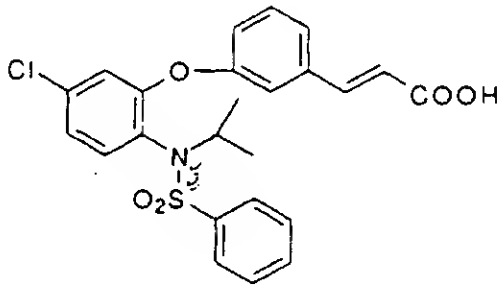


TLC : Rf 0.36 ($CHCl_3$: MeOH = 9 : 1);
NMR : δ 8.11 (2H, d, J=8.6Hz), 7.8-7.7 (2H, m), 7.6-7.3 (3H, m), 7.2-7.1 (2H, m), 7.02 (2H, d, J=8.6Hz), 6.92 (1H, d, J=2.0Hz), 4.6-4.4 (1H, m), 1.14 (3H, d, J=2.4Hz), 1.11 (3H, d, J=2.4Hz).

Example 18(37)

3-[2-(N-isopropyl-phenylsulfonylamino)-5-chlorophenoxy]cinnamic acid

[0247]

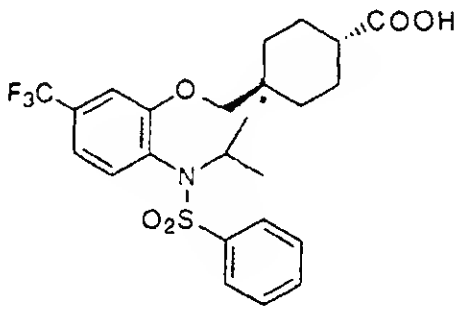


TLC : Rf 0.33 ($CHCl_3$: MeOH = 9 : 1);
NMR : δ 7.9-7.8 (2H, m), 7.73 (1H, d, J=15.8Hz), 7.6-7.3 (5H, m), 7.2-7.0 (4H, m), 6.78 (1H, d, J=2.2Hz), 6.42 (1H, d, J=15.8Hz), 4.6-4.4 (1H, m), 1.17 (3H, d, J=6.8Hz), 1.13 (3H, d, J=6.8Hz).

Example 18(38)

trans-4-[2-(N-isopropyl-phenylsulfonylamino)-5-trifluoromethylphenoxymethyl]cyclohexanoic acid

[0248]

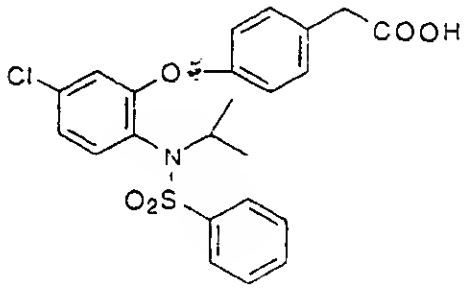


TLC : Rf 0.53 ($CHCl_3$: MeOH : AcOH= 100 : 5 : 1);
NMR : δ 7.81 (2H, m), 7.42-7.63 (3H, m), 7.10-7.24 (3H, m), 4.38 (1H, sept, J=6.8Hz), 3.79 (2H, m), 2.33 (1H, tt, J=3.8, 10.2Hz), 2.11 (2H, m), 1.93 (2H, m), 1.71 (1H, m), 1.50 (2H, m), 1.18 (2H, m), 1.07 (3H, d, J=6.8Hz), 1.02 (3H, d, J=6.8Hz).

Example 18(39)

4-[2-(N-isopropyl-phenylsulfonylamino)-5-chlorophenoxy]phenylacetic acid

[0249]

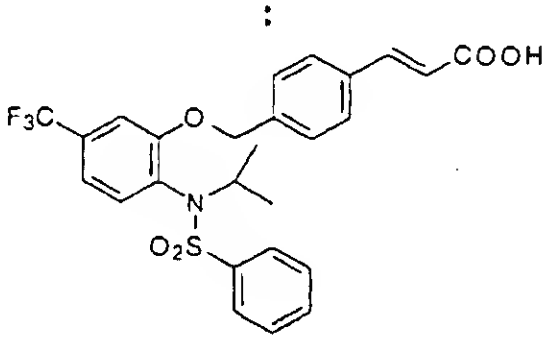


TLC : Rf 0.43 ($CHCl_3$: MeOH = 9 : 1);
NMR : δ 7.9-7.8 (2H, m), 7.6-7.4 (3H, m), 7.28 (2H, d, J=7.4Hz), 7.13 (1H, d, J=8.6Hz), 7.01 (1H, dd, J=2.2, 8.6Hz), 6.89 (2H, d, J=8.6Hz), 6.78 (1H, d, J=2.2Hz), 4.6-4.4 (1H, m), 3.66 (2H, s), 1.15 (3H, s), 1.12 (3H, s).

Example 18(40)

4-[2-(N-isopropyl-phenylsulfonylamino)-5-trifluoromethylphenoxymethyl]cinnamic acid

[0250]

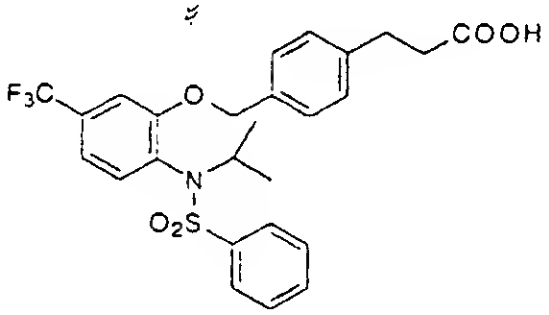


TLC : Rf 0.5 ($CHCl_3$: MeOH = 9 : 1);
NMR : δ 7.9-7.8 (3H, m), 7.60 (2H, d, J=8.0Hz), 7.5-7.3 (5H, m), 7.3-7.2 (3H, m), 6.49 (1H, d, J=15.8Hz), 5.08 (2H, s), 4.4-4.3 (1H, m), 1.05 (6H, d, J=6.6Hz).

Example 18(41)

3-[4-[2-(N-isopropyl-phenylsulfonylamino)-5-trifluoromethylphenoxymethyl]phenyl]propionic acid

[0251]

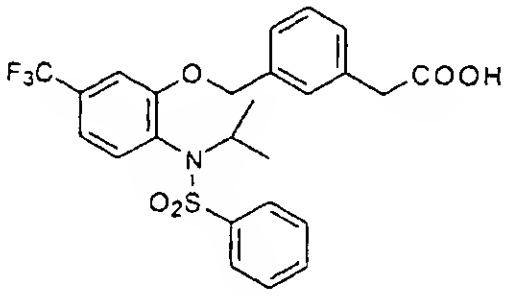


TLC: Rf 0.59 ($CHCl_3$: MeOH = 9 : 1);
NMR : δ 7.80 (2H, d, J=7.4Hz), 7.5-7.4 (1H, m), 7.4-7.2 (9H, m), 4.99 (2H, s), 4.4-4.2 (1H, m), 3.00 (2H, t, J=7.6Hz), 2.72 (2H, t, J=7.6Hz), 1.08 (3H, d, J=6.8Hz), 1.02 (3H, d, J=6.8Hz).

Example 18(42)

3-[2-(N-isopropyl-phenylsulfonylamino)-5-trifluoromethylphenoxymethyl]phenylacetic acid

[0252]

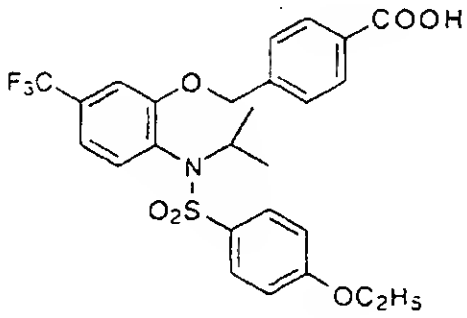


TLC : Rf 0.50 ($CHCl_3$: MeOH = 9 : 1);
NMR : δ 7.8-7.7 (2H, m), 7.6-7.2 (10H, m), 5.05 (1H, d, J=11.0Hz), 4.98 (1H, d, J=11.0Hz), 4.4-4.2 (1H, m), 3.68 (2H, s), 1.06 (3H, d, J=6.6Hz), 1.03 (3H, d, J=6.6Hz).

Exemple 18(43)

4-[2-(N-isopropyl-4-ethoxyphenylsulfonylamino)-5-trifluoromethylphenoxymethyl]benzoic acid

[0253]

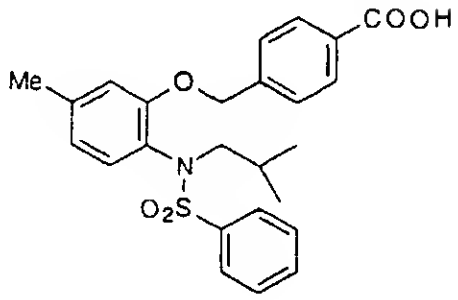


TLC : Rf 0.44 ($CHCl_3$: MeOH = 9 : 1);
NMR : δ 8.15 (2H, d, J=8.2Hz), 7.71 (2H, d, J=8.8Hz), 7.54 (2H, d, J=8.2Hz), 7.3-7.2 (3H, m), 6.78 (2H, d, J=8.8Hz), 5.14 (2H, s), 4.4-4.2 (1H, m), 4.03 (2H, q, J=7.0Hz), 1.44 (3H, t, J=7.0Hz), 1.08 (3H, d, J=7.0Hz), 1.04 (3H, d, J=7.0Hz).

Example 18(44)

4-[2-(N-isobutyl-phenylsulfonylamino)-5-methylphenoxymethyl]benzoic acid

[0254]

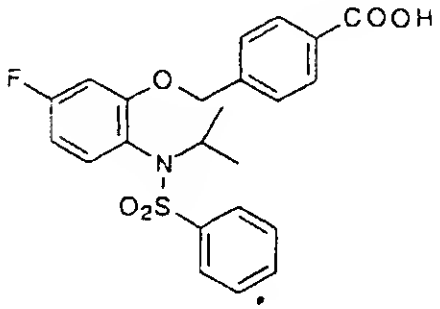


TLC : Rf 0.47 ($CHCl_3$: MeOH : AcOH= 100 : 5 : 1);
NMR : δ 8.07 (2H, d, J=8.2Hz), 7.63 (2H, m), 7.15-7.44 (6H, m), 6.79 (1H, m), 6.65 (1H, m), 4.80 (2H, m), 3.40 (2H, m), 2.33 (3H, s), 1.63 (1H, m), 0.90 (6H, d, J=6.4Hz).

Example 18(45)

4-[2-(N-isopropyl-phenylsulfonylamino)-5-fluorophenoxymethyl]benzoic acid

[0255]

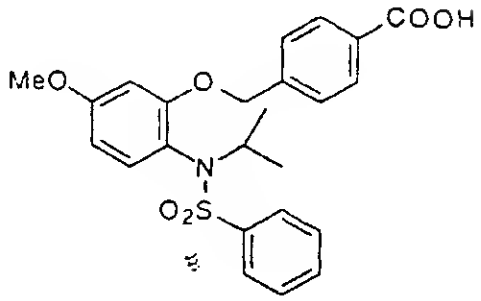


TLC : Rf 0.33 ($CHCl_3$: MeOH = 20 : 1);
NMR (DMSO-d_6) : δ 7.95 (2H, d, J=8.2Hz), 7.80 (2H, d, J=7.2Hz), 7.46-7.65 (5H, m), 7.08 (2H, m), 6.82 (1H, m), 5.14 (2H, bs), 4.20 (1H, sept, J=6.6Hz), 0.94 (6H, d, J=6.6Hz).

Example 18(46)

4-[2-(N-isopropyl-phenylsulfonylamino)-5-methoxyphenoxymethyl]benzoic acid

[0256]

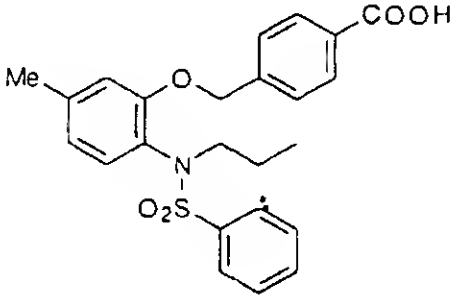


TLC : Rf 0.30 ($CHCl_3$: MeOH = 20 : 1);
NMR ($DMSO-d_6$) : δ 7.95 (2H, d, J=8.2Hz), 7.73 (2H, d, J=7.2Hz), 7.42-7.68 (3H, m), 6.93 (2H, d, J=8.6Hz), 7.21 (1H, m), 6.56 (2H, dd, J=8.6Hz, J=2.8Hz), 5.11 (2H, bs), 4.20 (1H, sept, J=6.6Hz), 3.79 (3H, s), 0.94 (6H, d, J=6.6Hz).

Example 18(47)

4-[2-(N-propyl-phenylsulfonylamino)-5-methylphenoxymethyl]benzoic acid

[0257]

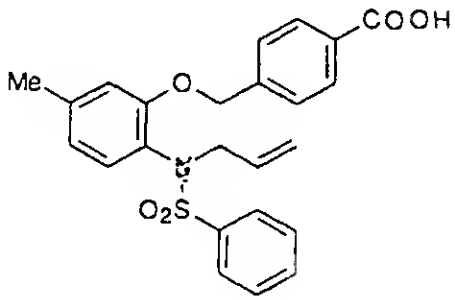


TLC : Rf 0.38 ($CHCl_3$: MeOH : AcOH= 100 : 5 : 1).
NMR : δ 8.07 (2H, d, J=8.6Hz), 7.67 (2H, m), 7.15-7.45 (6H, m), 6.79 (1H, m), 6.68 (1H, m), 4.83 (2H, brs), 3.57 (2H, m), 2.34 (3H, s), 1.48 (2H, m), 0.88 (3H, t, J=7.4Hz)

Example 18(48)

4-[2-[N-(prop-2-enyl)-phenylsulfonylamino]-5-methylphenoxymethyl]benzoic acid

[0258]

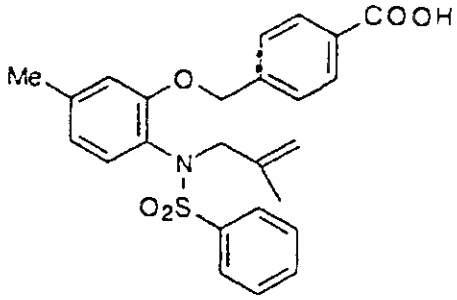


TLC : Rf 0.39 ($CHCl_3$: MeOH : AcOH= 100 : 5 : 1);
NMR : δ 8.07 (2H, d, J=8.0Hz), 7.69 (2H, m), 7.13-7.48 (6H, m), 6.78 (1H, m), 6.66 (1H, m), 5.80 (1H, tdd, J=6.2, 10.2, 17.2Hz), 4.98-5.12 (2H, m), 4.84 (2H, brs), 4.23 (2H, m), 2.33 (3H, s).

Example 18(49)

4-[2-[N-(2-methylprop-2-enyl)-phenylsulfonylamino]-5-methylphenoxymethyl]benzoic acid

[0259]

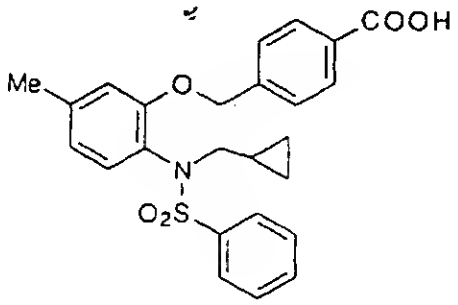


TLC : Rf 0.37 ($CHCl_3$: MeOH : AcOH= 100 : 5 : 1);
NMR : δ 8.07 (2H, d, J=8.2Hz), 7.66 (2H, m), 7.16-7.47 (6H, m), 6.77 (1H, m), 6.64 (1H, m), 4.80 (2H, brs), 4.71 (2H, m), 4.20 (1H, brs), 2.32 (3H, s), 1.77 (3H, s).

Example 18(50)

4-[2-(N-cyclopropylmethyl-phenylsulfonylamino)-5-methylphenoxymethyl]benzoic acid

[0260]

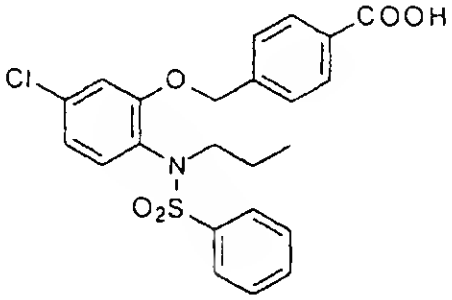


TLC : Rf 0.31 ($CHCl_3$: MeOH : AcOH= 100 : 5 : 1);
NMR : δ 8.06 (2H, d, J=8.0Hz), 7.68 (2H, m), 7.18-7.44 (6H, m), 6.80 (1H, m), 6.68 (1H, m), 4.84 (2H, brs), 3.48 (2H, m), 2.34 (3H, s), 0.91 (1H, m), 0.38 (2H, m), 0.07 (2H, m).

Example 18(51)

4-[2-(N-propyl-phenylsulfonylamino)-5-chlorophenoxymethyl]benzoic acid

[0261]

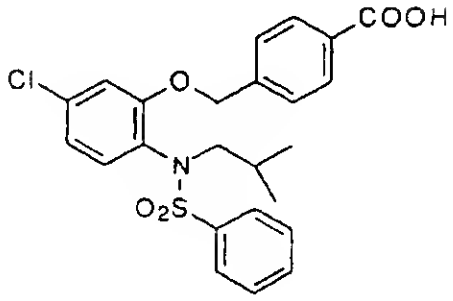


TLC : Rf 0.32 ($CHCl_3$: MeOH = 20 : 1);
NMR : δ 8.07 (2H, d, J=7.8Hz), 7.64 (2H, d, J=6.8Hz), 7.10-7.41 (6H, m), 6.85-6.99 (2H, m), 4.82 (2H, bs), 3.55 (2H, t, J=6.8Hz), 1.35-1.52 (2H, m), 0.87 (3H, t, J=7.6Hz).

Example 18(52)

4-[2-(N-isobutyl-phenylsulfonylamino)-5-chlorophenoxymethyl]benzoic acid

[0262]

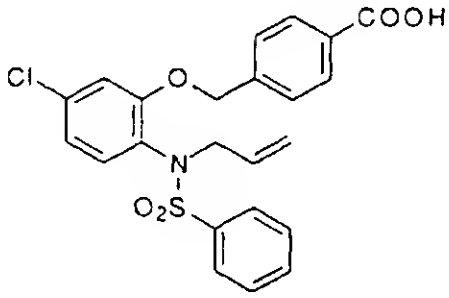


TLC : Rf 0.32 ($CHCl_3$: MeOH = 20 : 1);
NMR : δ 8.04 (2H, d, J=7.8Hz), 7.54 (2H, d, J=7.4Hz), 7.10-7.41 (6H, m), 6.80-7.01 (2H, m), 4.58-4.95 (2H, bs), 3.34 (2H, d, J=7.0Hz), 1.46-1.65 (1H, m), 0.83 (6H, d, J=6.4Hz).

Example 18(53)

4-[2-[N-(prop-2-enyl)-phenylsulfonylamino]-5-chlorophenoxymethyl]benzoic acid

[0263]

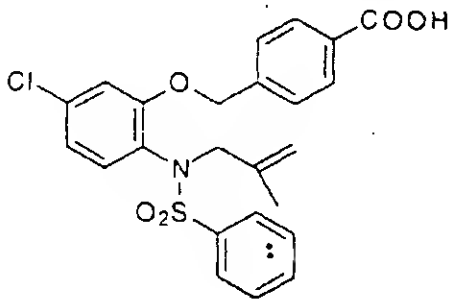


TLC : Rf 0.30 ($CHCl_3$: MeOH = 20 : 1),
NMR · δ 8.09 (2H, d, J=8.2Hz), 7.68 (2H, d, J=6.8Hz), 7.19-7.52 (6H, m), 6.87-7.01 (2H, m), 5.76 (1H, ddt, J=17.2Hz, 9.8Hz, 6.4Hz) 5.09 (1H, d, J=17.2Hz), 5.07 (1H ,d , J=9.8Hz), 4.85 (2H, s), 4.21 (2H, d, J=6.4Hz).

Example 18(54)

4-[2-[N-(2-methylprop-2-enyl)-phenylsulfonylamino]-5-chlorophenoxymethyl]benzoic acid

[0264]

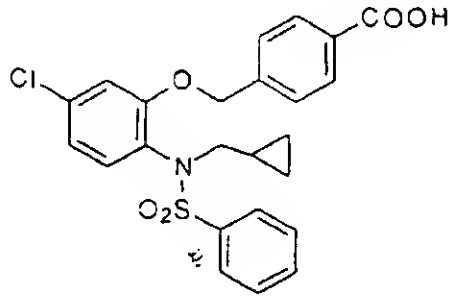


TLC : Rf 0.33 ($CHCl_3$: MeOH = 20 : 1);
NMR : δ 8.09 (2H, d, J=8.2Hz), 7.65 (2H, d, J=6.8Hz), 7.21-7.51 (6H, m), 6.83-7.00 (2H, m), 4.81 (2H, s), 4.74 (1H, s), 4.68 (1H, s), 4.18 (2H,s), 1.75 (3H, s).

Example 18(55)

4-[2-(N-cyclopropylmethyl-phenylsulfonylamino)-5-chlorophenoxymethyl]benzoic acid

[0265]

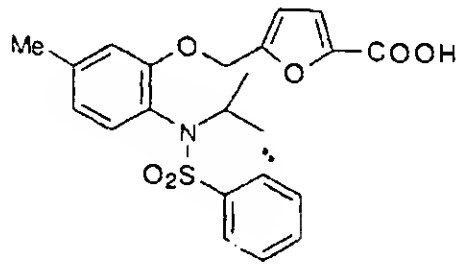


TLC : Rf 0.40 ($CHCl_3$: MeOH = 20 : 1);
NMR : δ 8.07 (2H, d, J=8.6Hz), 7.69 (2H, d, J=7.0Hz), 7.20-7.48 (6H, m), 6.85-7.09 (2H, m), 4.85(2H, s), 3.47 (2H, bs), 0.85 (1H, m), 0.38 (2H, m), 0.06 (2H, m).

Example 18(56)

5-[2-(N-isopropyl-phenylsulfonylamino)-5-methylphenoxymethyl]furan-2-carboxylic acid

[0266]

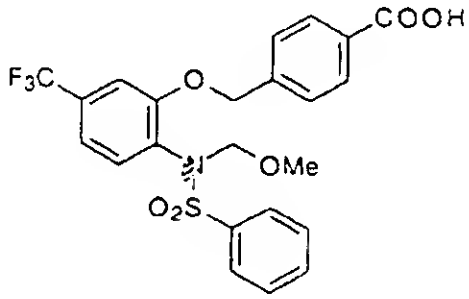


TLC : Rf 0.18 ($CHCl_3$: MeOH = 9 : 1);
NMR : δ 7.82 (2H, m), 7.56-7.35 (3H, m), 7.31 (1H, d, J =3.5Hz), 6.97 (1H, d, J=8.5Hz), 6.83-6.75 (2H, m), 6.63 (1H, d, J=3.5Hz), 5.03 (1H, d, J=14Hz), 4.98 (1H, d, J=14Hz), 4.37 (1H, m) , 2.37 (3H, s), 1.09-0.96 (6H, m).

Example 18(57)

4-[2-(N-methoxymethyl-phenylsulfonylamino)-5-trifluoromethylphenoxymethyl]benzoic acid

[0267]

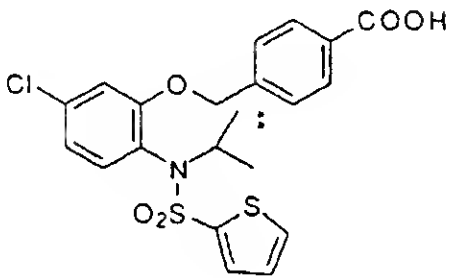


TLC : Rf 0.45 ($CHCl_3$: MeOH : AcOH= 100 : 5 : 1);
NMR : δ 8.09 (2H, d, J=8.0Hz), 7.65 (2H, m), 7.43-7.53 (2H, m), 7.20-7.40 (5H, m), 7.11 (1H, m), 5.09 (2H, s), 4.89 (2H, s), 3 44 (3H, s).

Example 18(58)

4-[2-(N-isopropyl-2-thienylsulfonylamino)-5-chlorophenoxymethyl]benzoic acid

[0268]

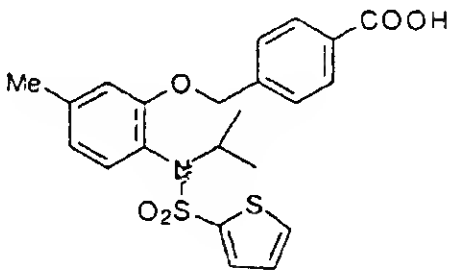


TLC : Rf 0.34 ($CHCl_3$: MeOH = 20 : 1);
NMR : δ 8.14 (2H, d, J=8.2Hz), 7.52-7.57 (4H, m), 6.98-7.03 (4H, m), 5.12 (2H, s), 4.55 (1H, sept, J=6.4Hz), 1.09 (6H, d, J=6.6Hz).

Example 18(59)

4-[2-(N-isopropyl-2-thienylsulfonylamino)-5-methylphenoxymethyl]benzoic acid

[0269]

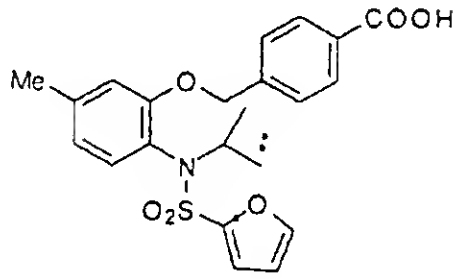


TLC : Rf 0.39 ($CHCl_3$: MeOH = 20 : 1);
NMR : δ 8 13 (2H, d, J=8.2Hz),7.43-7 58 (4H, m), 6.97 (1H, m), 6.80 (2H, m), 5.12 (2H, s), 4.45 (1H, sept, J=6.4Hz), 1.09 (6H, d, J=6.6Hz).

Example 18(60)

4-[2-(N-isopropyl-2-furanylsulfonylamino)-5-methylphenoxymethyl]benzoic acid

[0270]

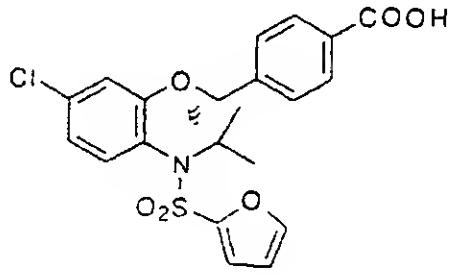


TLC : Rf 0.42 ($CHCl_3$: MeOH : AcOH= 100 : 5 : 1);
NMR : δ 8.14 (2H, d, J=8.2Hz), 7.58 (2H, d, J=8.2Hz), 7.44 (1H, dd, J=0.8, 1.6Hz), 6.88-6.95 (2H, m), 6.72-6.82 (2H, m), 6.41 (1H, dd, J=1.6, 3.4Hz), 5.12 (2H, s), 4.51 (1H, sept, J=6.6Hz), 2.31 (3H, s), 1.12 (3H, d, J=6.6Hz), 1.10 (3H, d, J=6.6Hz).

Example 18(61)

4-[2-(N-isopropyl-2-furanylsulfonylamino)-5-chlorophenoxymethyl]benzoic acid

[0271]

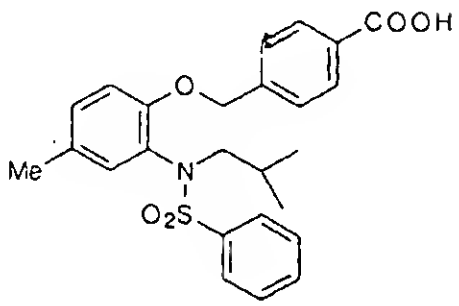


TLC : Rf 0.43 ($CHCl_3$: MeOH : AcOH= 100 : 5 : 1);
NMR : δ 8.16 (2H, d, J=8.4Hz), 7.57 (2H, d, J=8.4Hz), 7.45 (1H, dd, J=0.8, 1.6Hz), 6.95-7.04 (3H, m), 6.92 (1H, d, J=4.4Hz), 6.43 (1H, dd, J=1.8, 3.4Hz), 5.13 (2H, s), 4.49 (1H, sept, J=7.0Hz), 1.11 (3H, d, J=7.0Hz), 1.09 (3H, d, J=7.0Hz).

Example 18(62)

4-[2-(N-isobutyl-phenylsulfonylamino)-4-methylphenoxymethyl]benzoic acid

[0272]

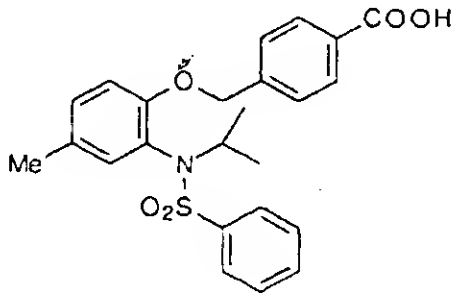


TLC : Rf 0.23 (hexane : AcOEt = 1 : 1);
NMR : δ 8.06 (2H, d, J=8Hz), 7.65-7.61 (2H, m), 7.6-7.4 (7H, m), 6.71 (1H, d, J=8Hz), 4.9-4.6 (2H, m), 3.5-3.4 (2H, m), 2.29 (3H, s), 1.63 (1H, sept., J=6.5 Hz), 0.91 (6H, d, J=6.5Hz).

Example 18(63)

4-[2-(N-isopropyl-phenylsulfonylamino)-4-methylphenoxymethyl]benzoic acid

[0273]

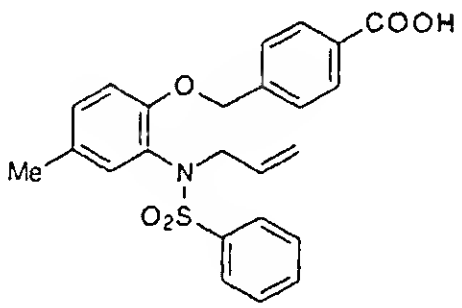


TLC : Rf 0.22 (hexane : AcOEt = 1 : 1);
NMR : δ 8.12 (2H, d, J=8Hz), 7.86-7.81 (2H, m), 7.52-7.30 (5H, m), 7.15-7.10 (1H, m), 6.94 (1H, d, J=1.5Hz), 6.84 (1H, d, J=8Hz), 5.02 (2H, s), 4.37 (1H, sept., J=6.5 Hz), 2.28 (3H, s), 1.08 (6H, t, J=6.5 Hz).

Example 18(64)

4-[2-[N-(prop-2-enyl)-phenylsulfonylamino]-4-methylphenoxymethyl]benzoic acid

[0274]

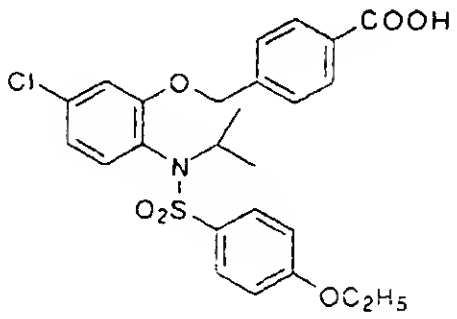


TLC : Rf 0.43 ($CHCl_3$: MeOH : AcOH= 100 : 5 : 1);
NMR (DMSO-d_6) : δ 7.89 (2H, d, J=8.2Hz), 7.63 (2H, m), 7.38-7.59 (3H, m), 7.23 (2H, d, J=8.2Hz), 7.12 (1H, dd, J=1.8, 8.4Hz), 6.98 (1H, d, J=1.8Hz), 6.94 (1H, d, J=8.6Hz), 5.71 (1H, tdd, J=6.4, 10.0, 17.2Hz), 4.97-5.13 (2H, m), 4.88 (2H, brs), 4.17 (2H, m), 2.22 (3H, s).

Example 18(65)

4-[2-(N-isopropyl-4-ethoxyphenylsulfonylamino)-5-chlorophenoxymethyl]benzoic acid

[0275]

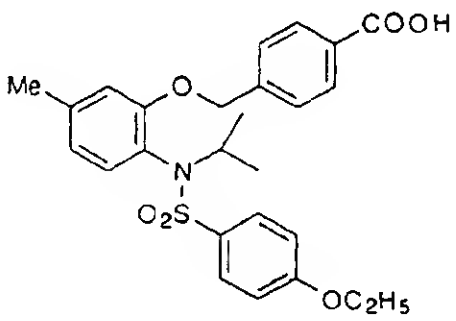


TLC : Rf 0.33 ($CHCl_3$: MeOH = 20 : 1);
NMR : δ 8.13 (2H, d, J=8.6Hz), 7.69 (2H, d, J=9.0Hz), 7.49 (2H, d, J=8.6Hz), 6.97-7.09 (3H, m), 6.76 (2H, d, J=9.0Hz), 5.06 (2H, s), 4.34 (1H, sept, J=6.6Hz), 4.02 (2H, q, J=7.2Hz), 1.43 (3H, t, J=7.0Hz), 1.06 (3H, d, J=6.6Hz), 1.03 (3H, d, J=6.6Hz).

Example 18(66)

4-[2-(N-isopropyl-4-ethoxyphenylsulfonylamino)-5-methylphenoxymethyl]benzoic acid

[0276]

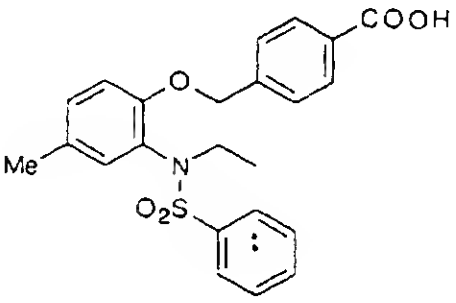


TLC : Rf 0.29 ($CHCl_3$: MeOH = 20 : 1);
NMR : δ 8.12 (2H, d, J=8.4Hz), 7.72 (2H, d, J=8.6Hz), 7.50 (2H, d, J=8.6Hz), 7.01 (1H, d, J=8.8Hz), 6.72-6.80 (4H, m), 5.07 (2H, s), 4.34 (1H, sept, J=6.6Hz), 4.01 (2H, q, J=7.0Hz), 2.36 (3H, s), 1.42 (3H, t, J=6.8Hz), 1.07 (3H, d, J=7.2Hz), 1.04 (3H, d, J=6.8Hz).

Example 18(67)

4-[2-(N-ethyl-phenylsulfonylamino)-4-methylphenoxymethyl]benzoic acid

[0277]

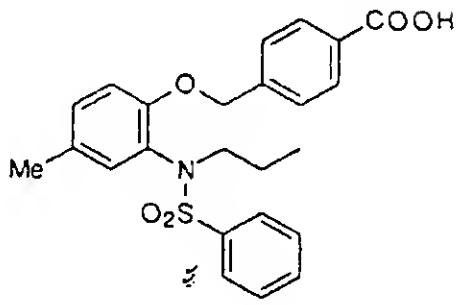


TLC : Rf 0.33 ($CHCl_3$: MeOH = 9 : 1);
NMR : δ 8.05 (2H, d, J=8.4Hz), 7.8-7.6 (2H, m), 7.4-7.2 (5H, m), 7.2-7.0 (2H, m), 6.75 (1H, d, J=8.4Hz), 4.82 (2H, s), 3.8-3.6 (2H, m), 2.30 (3H, s), 1.11 (3H, t, J=7.0Hz).

Example 18(68)

4-[2-(N-propyl-phenylsulfonylamino)-4-methylphenoxymethyl]b nzoic acid

[0278]

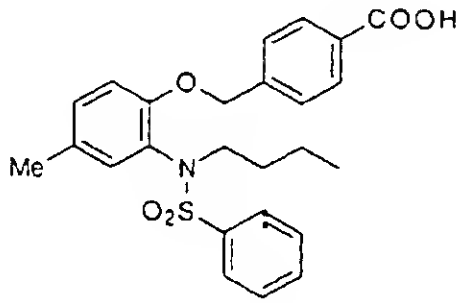


TLC : Rf 0.44 ($CHCl_3$: MeOH = 9 : 1);
NMR : δ 8.05 (2H, d, J=8.0Hz), 7.7-7.6 (2H, m), 7.5-7.0 (7H, m), 6.74 (1H, d, J=8.4Hz), 4.80 (2H, s), 3.7-3.5 (2H, m), 2.29 (3H, s), 1.6-1.4 (2H, m), 0.89 (3H, t, J=7.4Hz).

Example 18(69)

4-[2-(N-butyl-phenylsulfonylamino)-4-methylphenoxymethyl]benzoic acid

[0279]

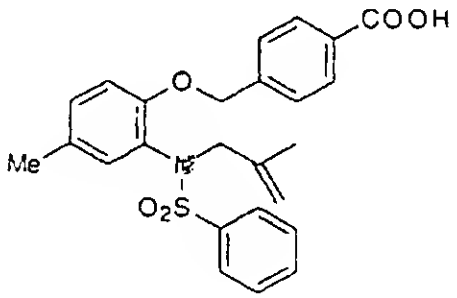


TLC Rf 0.49 ($CHCl_3$: MeOH = 9 : 1);
NMR : δ 8.05 (2H, d, J=8.2Hz), 7.7-7.6 (2H, m), 7.4-7.2 (5H, m), 7.2-7.0 (2H, m), 6.74 (1H, d, J=8.4Hz), 4.80 (2H, s), 3.7-3.5 (2H, m), 2.30 (3H, s), 1.6-1.2 (4H, m), 0.85 (3H, t, J=7.0Hz).

Example 18(70)

4-[2-[N-(2-methylprop-2-enyl)-phenylsulfonylamino]-4-methylphenoxymethyl]benzoic acid

[0280]

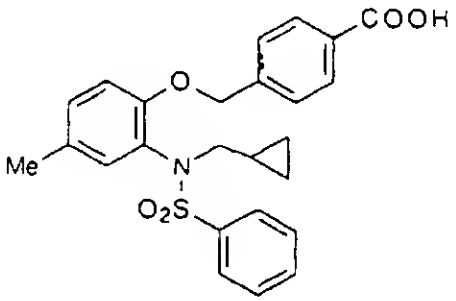


TLC : Rf 0.38 ($CHCl_3$: MeOH = 9 : 1);
NMR : δ 8.06 (2H, d, J=8Hz), 7.65 (2H, m), 7.47-7.25 (3H, m), 7.19 (2H, d, J=8Hz), 7.13 (1H, d, J=2Hz), 7.04 (1H, dd, J=8 and 2Hz), 6.70 (1H, d, J=8Hz), 4.85-4.65 (4H, m), 4.21 (2H, s), 2.29 (3H, s), 1.78 (3H, s).

Example 18(71)

4-[2-(N-cyclopropylmethyl-phenylsulfonylamino)-4-methylphenoxymethyl]benzoic acid

[0281]

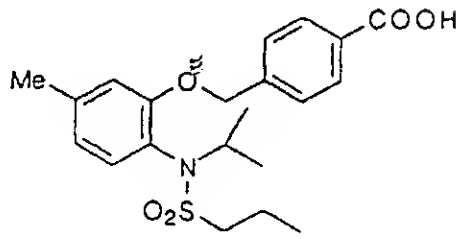


TLC : Rf 0 40 ($CHCl_3$: MeOH : AcOH= 100 : 5 : 1);
NMR (CD_3COCD_3) : δ 7.99(2H, d, J=8.0Hz), 7.68 (2H, m), 7.26-7.57 (5H, m), 7.15 (2H, m), 6.96 (1H, d, J=8.8Hz), 4.93 (2H, brs), 3.52 (2H, brd, J=7.0Hz), 2.28 (3H, s), 0.90 (1H, m), 0.35 (2H, m), 0.06 (2H, m).

Example 18(72)

4-[2-(N-isopropyl-propylsulfonylamino)-5-methylphenoxymethyl]benzoic acid

[0282]

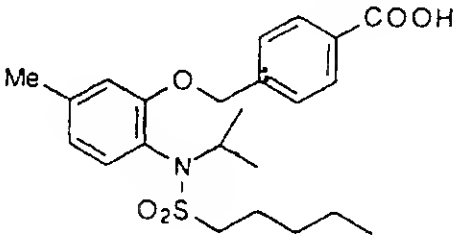


TLC : Rf 0.24 ($CHCl_3$: MeOH = 19 : 1);
NMR : δ 8.14 (2H, d, J=8.2Hz), 7.57 (2H, d, J=8.2Hz), 7.16 (1H, m), 6.82 (2H, m), 5.13 (2H, s), 4.33 (1H, m), 2.97 (2H, m), 2.36 (3H, s), 1.79 (2H, m), 1.23 (3H, d, J=6.6Hz), 1.09 (3H, d, J=6.6Hz), 0.85 (3H, t, J=7.4Hz).

Example 18(73)

4-[2-(N-isopropyl-pentylsulfonylamino)-5-methylphenoxymethyl]benzoic acid

[0283]

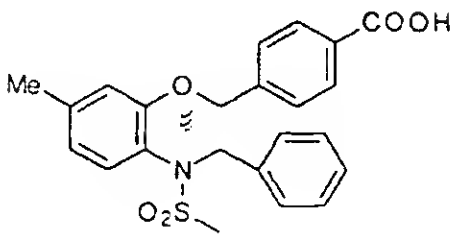


TLC : Rf 0.26 ($CHCl_3$: MeOH = 19 : 1);
NMR : δ 8.15 (2H, d, J=8.0Hz), 7.56 (2H, d, J=8.0Hz), 7.14 (1H, m), 6.81 (2H, m), 5.12 (2H, s), 4.32 (1H, m), 2.97 (2H, m), 2.36 (3H, s), 1.77 (2H, m), 1.24 (3H, d, J=6.6Hz), 1.16 (4H, m), 1.09 (3H, d, J=6.6Hz), 1.12 (3H, d, J=6.6Hz), 0.83 (3H, t, J=6.4Hz).

Example 18(74)

4-[2-(N-benzyl-methylsulfonylamino)-5-methylph noxymethyl]benzoic acid

[0284]

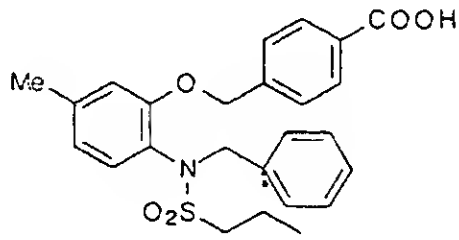


TLC : Rf 0.39 ($CHCl_3$: MeOH = 19 : 1);
NMR : δ 8.17 (2H, d, J=8.0Hz), 7.53 (2H, d, J=8.0Hz), 7.25 (5H, s), 6.98 (1H, m), 6.77 (2H, m), 5.17 (2H, s), 4.70 (2H, bs), 2.89 (3H, s), 2.30 (3H, s).

Example 18(75)

4-[2-(N-benzyl-propylsulfonylamino)-5-methylphenoxymethyl]benzoic acid

[0285]

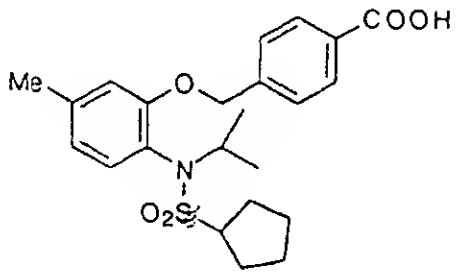


TLC : Rf 0.40 ($CHCl_3$: MeOH = 19 : 1);
NMR : δ 8 17 (2H, d, J=8.2Hz), 7.55 (2H, d, J=8 2Hz), 7 23 (5H, s), 6.98 (1H, m), 6.78 (2H, m), 5.16 (2H, s), 4.77 (2H, bs), 2 95 (2H, m), 2.29 (3H, s), 1.81 (2H, m), 0.85 (3H, t, J=7.6Hz).

Example 18(76)

4-[2-(N-isopropyl-cyclopentylsulfonylamino)-5-methylphenoxymethyl]benzoic acid

[0286]

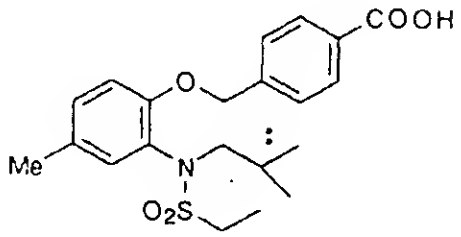


TLC : Rf 0.38 ($CHCl_3$: MeOH : AcOH= 100 : 5 : 1);
NMR : δ 8.15 (2H, d, J=8.0Hz), 7.59 (2H, d, J=8.0Hz), 7.14 (1H, d, J=8.6Hz), 6.81 (2H, m), 5.12 (2H, s), 4.35 (1H, sept, J=6.6Hz), 3.51 (1H, m), 2.36 (3H, s), 1.85-2.15 (3H, m), 1.61-1.85 (3H, m), 1.34-1.61 (2H, m), 1.22 (3H, d, J=6.6Hz), 1.08 (3H, d, J=6.6Hz).

Example 18(77)

4-[2-(N-isobutyl-ethylsulfonylamino)-4-methylphenoxymethyl]benzoic acid

[0287]

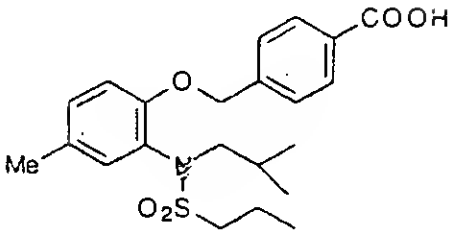


TLC : Rf 0.23 (hexane : AcOEt = 1 : 1);
NMR : δ 8.15 (2H, d, J=8Hz), 7.53 (2H, d, J=8Hz), 7.21 (1H, d, J=1.5Hz), 7.08 (1H, dd, J=8.5, 1.5Hz), 6.86 (1H, d, J=8.5Hz), 5.17 (2H, s), 3.46 (2H, d, J=7.5Hz), 2.97 (2H, q, J=7.5Hz), 2.30 (3H, s), 1.7-1 .5 (1H, m), 1.25 (3H, t, J=7 5Hz), 0.94-0.90 (6H, m)

Example 18(78)

4-[2-(N-isobutyl-propylsulfonylamino)-4-methylphenoxymethyl]benzoic acid

[0288]

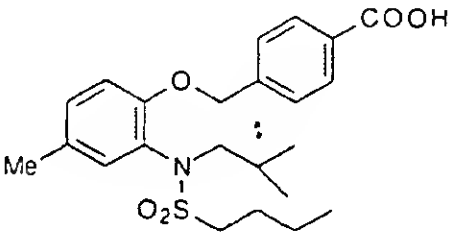


TLC : Rf 0.27 (hexane : AcOEt = 1 : 1);
NMR : δ 8.15 (2H, d, J=8Hz), 7.53 (2H, d, J=8Hz), 7.20 (1H, d, J=0.5Hz), 7.03 (1H, dd, J=8, 0.5Hz), 6.86 (1H, d, J=8Hz), 5.17 (2H, s), 3.44 (2H, d, J=7Hz), 2.94-2.86 (2H, m), 2.30 (3H, s), 1.9-1.6 (3H, m), 1 .0-0.9(6H, m), 0.85 (3H, t, J=7Hz).

Example 18(79)

4-[2-(N-isobutyl-butylsulfonylamino)-4-methylphenoxymethyl]benzoic acid

[0289]

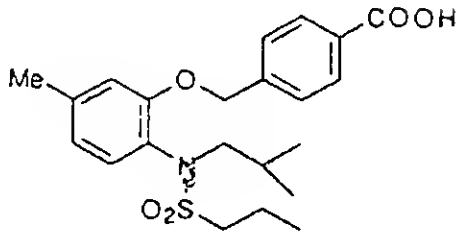


TLC : Rf 0.37 (hexane : AcOEt = 1 : 1);
NMR : δ 8.15 (2H, d, J=8Hz), 7.53 (2H, d, J=8Hz), 7.20 (1H, d, J=0.5Hz), 7.08 (1H, dd, J=8.5, 0.5Hz), 6.86 (1H, d, J=8.5Hz), 5.16 (2H, s), 3.45 (2H, d, J=7Hz), 2.97-2.89 (2H, m), 2.30 (3H, s), 1.8-1.5 (3H , m), 1.3-1.1 (2H, m), 1.0-0.9(6H, m), 0.79 (3H, t, J=7Hz)

Example 18(80)

4-[2-(N-isobutyl-propylsulfonylamino)-5-m thylphenoxymethyl]benzoic acid

[0290]

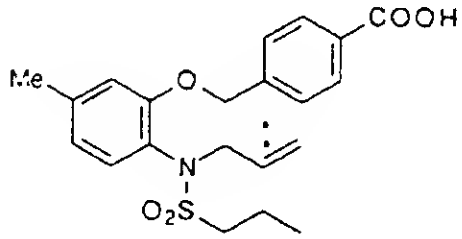


TLC : Rf 0.25 ($CHCl_3$: MeOH = 20 : 1);
NMR : δ 8.16 (2H, d, J=8.4Hz), 7.53 (2H, d, J=8.4Hz), 7.28 (1H, m), 6.82 (2H, m), 5.18 (2H, s), 3.41 (2H, d, J=7.0Hz) ,2.89 (2H, m), 2.35 (3H, s), 1.78 (2H, m), 1.60 (1H, m), 0.90 (6H, d, J=7.0Hz), 0.84 (3H, t, 7.6Hz).

Example 18(81)

4-[2-[N-(prop-2-enyl)-propylsulfonylamino]-5-methylphenoxymethyl]benzoic acid

[0291]

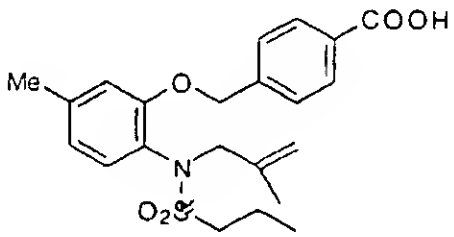


TLC : Rf 0.23 ($CHCl_3$: MeOH = 20 : 1);
NMR : δ 8 16 (2H, d, J=8.4Hz), 7.56 (2H, d, J=8.4Hz), 7.21 (1H, m), 6.90 (2H, m), 5.80 (1H, m), 5.17 (2H, s), 5.07 (2H, m), 4.21 (2H, d, J=6.2Hz), 2.94 (2H, m), 2.34 (3H, s), 1.81 (2H, m), 0.86 (3H, t, J=7.4Hz).

Example 18(82)

4-[2-[N-(2-methylprop-2-enyl)-propylsulfonylamino]-5-metnylphenoxymethyl]benzoic acid

[0292]

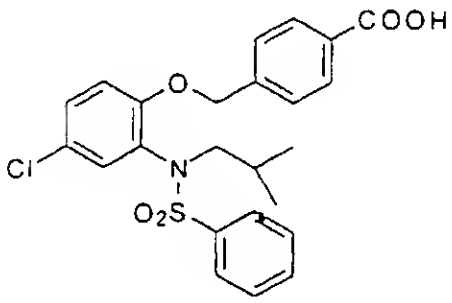


TLC : Rf 0.28 ($CHCl_3$: MeOH = 20 : 1);
NMR : δ 8.16 (2H, d, J=8.2Hz), 7.54 (2H, d, J=8.2Hz), 7.23 (1H, m), 6.78 (2H, m), 5.17 (2H, s), 4.75 (2H, s), 4.18 (2H, s), 2.88 (2H, m), 2.34 (3H, s), 1.79 (2H, m), 1.78 (3H, s), 0.85 (3H, t, J=7.6Hz).

Example 18(83)

4-[2-(N-isobutyl-phenylsulphonylamino)-4-chlorophenoxymethyl]benzoic acid

[0293]

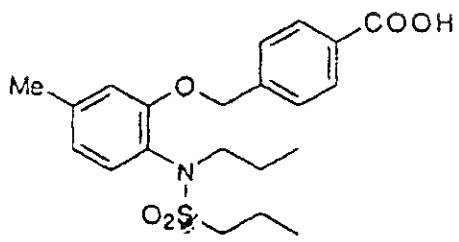


TLC : Rf 0.29 ($CHCl_3$: MeOH = 19 : 1);
NMR : δ 8.06 (2H, d, J=8.0Hz), 7.64 (2H, d, J=8.0Hz), 7.20-7.40 (7H, m), 6.78 (1H, m), 4.80 (2H, bs), 3.40 (2H, d, J=7.0Hz), 1.61 (1H, m), 0.90 (6H, d, J=7.0Hz).

Example 18(84)

4-[2-(N-propyl-propylsulfonylamino)-5-methylph noxymethyl]benzoic acid

[0294]

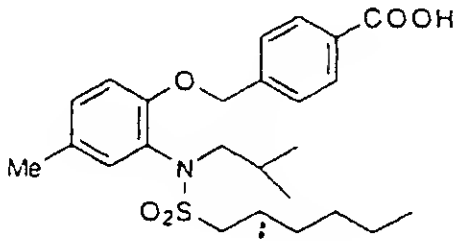


TLC : Rf 0.52 ($CHCl_3$: MeOH = 9 : 1);
NMR : δ 8.17 (2H, d, J=8.4Hz), 7.55 (2H, d, J=8.4Hz), 7.25 (1H, d, J=8.2Hz), 6.9-6.8 (2H, m), 5.17 (2H, s), 3.56 (2H, t, J=7.4Hz), 3.0-2.8 (2H, m), 2.35 (3H, s), 1.9-1.7 (2H, m), 1.6-1.4 (2H, m), 0.89 (3H, t, J=7.2Hz), 0.84 (3H, t, J=7.4Hz).

Example 18(85)

4-[2-(N-isobutyl-hexylsulfonylamino)-4-methylphenoxymethyl]benzoic acid

[0295]

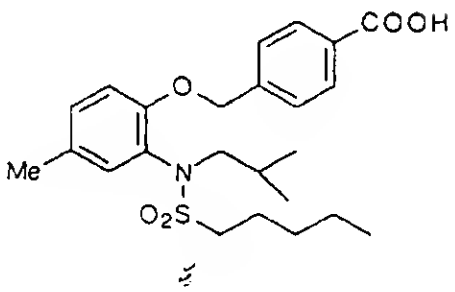


TLC : Rf 0.49 ($CHCl_3$: MeOH = 9 : 1);
NMR : δ 8.16 (2H, d, J=8.4Hz), 7.53 (2H, d, J=8.4Hz) 7.21 (1H, d, J=2.0Hz), 7.09 (1H, dd, J=2.0, 8.4Hz), 6.87 (1H, d, J=8.4Hz), 5.16 (2H, s), 3.45 (2H, d, J=7.0Hz), 3.0-2.8 (2H, m), 2.30 (3H, s), 1.8-1.5 (3H, m), 1.3-1.0 (6H, m), 1.0-0.8 (6H, m), 0.83 (3H, t, J=7.0Hz).

Example 18(86)

4-[2-(N-isobutyl-pentylsulfonylamino)-4-methylphenoxymethyl]benzoic acid

[0296]

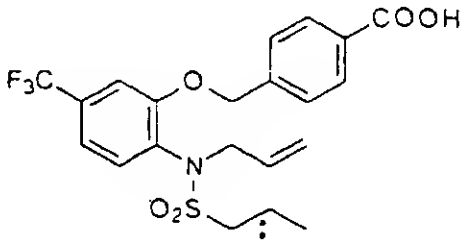


TLC : Rf 0.38 ($CHCl_3$: MeOH : AcOH= 100 : 5 : 1);
NMR : δ 8.16 (2H, d, J=8.4Hz), 7.53 (2H, d, J=8.4Hz), 7.21 (1H, d, J=2.2Hz), 7.09 (1H, dd, J=2.2, 8.6Hz), 6.87 (1H, d, J=8.6Hz), 5.16 (2H, s), 3.45 (2H, d, J=7.2Hz), 2.91 (2H, m), 2.30 (3H, s), 1.74 (2H, m), 1.60 (1H, m), 1.17 (4H, m), 0.92 (6H, m), 0.82 (3H, m).

Example 18(87)

4-[2-[N-(prop-2-enyl)-propylsulfonylamino]-5-trifluoromethylphenoxymethyl]benzoic acid

[0297]

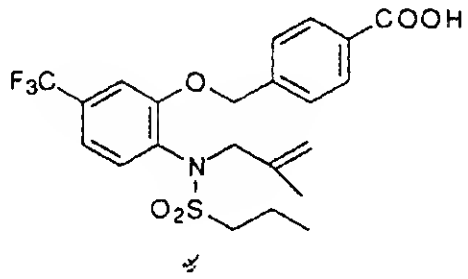


TLC : Rf 0.33 (hexane : AcOEt = 1 : 1),
NMR (200MHz, $CDCl_3$ + 1drop of CD_3OD) : δ 8.15-8.11 (2H, m), 7.54-7.44(3H, m), 7.30-7.24 (2H, m), 5.88-5.68 (1H, m), 5.20 (2H, s), 5.12-5.10 (1H, m), 5.04-5.03 (1H, m), 4.21 (2H, d, J=6.5Hz), 2.95-2.87 (2H, m), 1.8-1.7 (1H, m), 0.84 (3H, t, J=7.5 Hz).

Example 18(88)

4-[2-[N-(2-methylprop-2-enyl)-propylsulfonylamino]-5-trifluoromethylphenoxymethyl]benzoic acid

[0298]

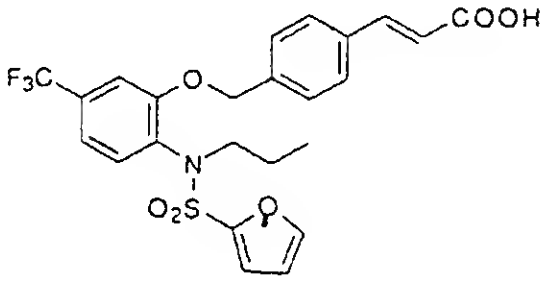


TLC : Rf 0.41 (hexane : AcOEt = 1 : 1);
NMR : δ 8.30 (2H, d, J=8Hz), 7.71-7.67 (2H, m), 7.62-7.56 (1H, m), 7.40-7.35 (2H, m), 5.34 (2H, s), 4.89-4.85 (2H, m), 5.34 (2H, s), 4.89-4.85 (2H, m), 4.31 (2H, s), 3.07-2.99 (2H, m), 2.0-1.8 (2H, m), 1.87 (3H, s), 1.00-0.93 (3H, m).

Example 18(89)

4-[2-(N-propyl-2-furanylsulfonylamino)-5-trifluoromethylphenoxymethyl]cinnamic acid

[0299]

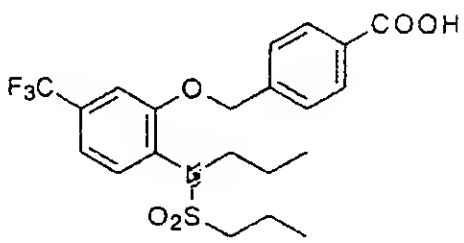


TLC : Rf 0.38 (hexane : AcOEt = 1 : 1);
NMR : δ 7.81 (1H, d, J=16Hz), 7.59 (2H, d, J=8Hz), 7.42-7.37 (3H, m), 7.28-7.24 (2H, m), 7.18 (1H, d, J=1.5Hz), 6.85 (1H, dd, J=3, 1Hz), 6.49 (1H, d, J=16Hz), 6.35 (1H, dd, J=3, 2Hz), 5.03 (2H, s), 3.71-3.64 (2H, m), 1.6-1.4 (2H, m), 0.88 (3H, t, J=7Hz).

Example 18(90)

4-[2-(N-propyl-propylsulfonylamino)-5-trifluoromethylphenoxymethyl]benzoic acid

[0300]

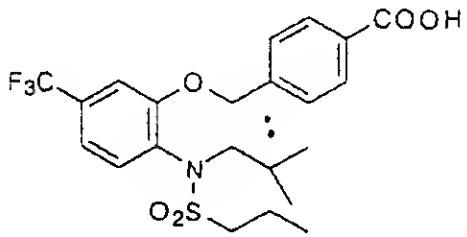


TLC : Rf 0.40 ($CHCl_3$: MeOH = 9 : 1);
NMR : δ 8.17 (2H, d, J=8.2Hz), 7.56 (2H, d, J=8.2Hz), 7.49 (1H, m), 7.27 (2H, m), 5.22 (2H, s), 3.58 (2H, m), 2.91 (2H, m), 1.79 (2H, m), 1.45 (2H, m), 0.89 (3H, t, J=7.4Hz), 0.85 (3H, t, J=7.6Hz).

Example 18(91)

4-[2-(N-isobutyl-propylsulfonylamino)-5-trifluoromethylphenoxymethyl]benzoic acid

[0301]

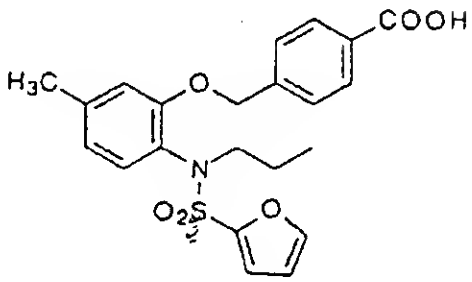


TLC : Rf 0.45 ($CHCl_3$: MeOH = 9 . 1);
NMR : δ 8.18 (2H, d, J=8.2Hz), 7 56 (2H, d, J=8.2Hz), 7.51 (1H, m), 7.28 (2H, m), 5.23 (2H, s), 3.45 (2H, d, J=7.4Hz), 2.89 (2H, m), 1.75 (2H, m), 1 58 (1H, m), 0.90 (6H, d, J=6.8Hz), 0.84 (3H, t, J=7.4Hz).

Example 18(92)

4-[2-(N-propyl-2-furanylsulfonylamino)-5-methylphenoxym thyl]benzoic acid

[0302]

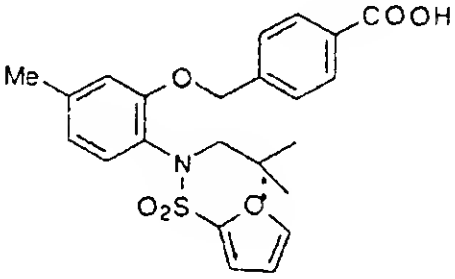


TLC : Rf 0.38 (hexane : AcOEt = 1 : 1);
NMR : δ 8.13 (2H, d, J=8Hz), 7.44 (2H, d, J=8Hz), 7.25 (1H, m), 7.12 (1H, d, J=8Hz), 6.83-6.73 (3H, m), 6.33-6.30 (1H, m), 5.01 (2H, s), 3.7-3.6 (2H, m), 2.33 (3H, s), 1.52 (2H, q, J=7Hz), 0.90 (3H, t, J=7Hz).

Example 18(93)

4-[2-(N-isobutyl-2-furanylsulfonylamino)-5-methylphenoxymethyl]benzoic acid

[0303]

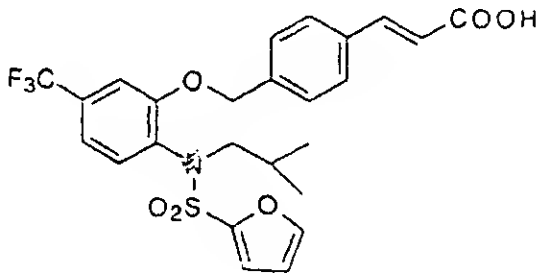


TLC . Rf 0.41 (hexane : AcOEt = 1 : 1);
NMR : δ 8.13 (2H, d, J=8Hz), 7.44 (2H, d, J=8Hz), 7.25 (1H, m), 7.15 (1H, d, J=8Hz), 6.80-6.71 (3H, m), 6.31 (1H, m), 5.0 (2H, m), 3.53 (2H, d, J=7Hz), 1.75-1.60(1H, m), 0.91 (6H, t, J=7Hz).

Example 18(94)

4-[2-(N-isobutyl-2-furanylsulfonylamino)-5-trifluoromethylphenoxymethyl]cinnamic acid

[0304]

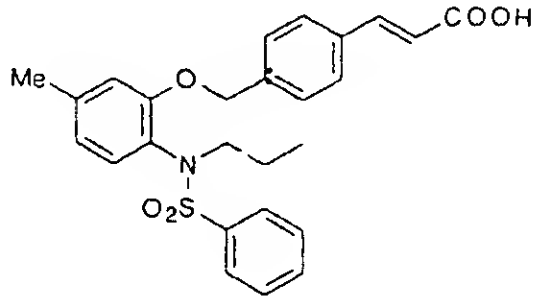


TLC : Rf 0.44 (hexane : AcOEt = 1 : 1);
NMR : δ 7.81 (1H, d, J=16Hz), 7.60 (2H, d, J=8Hz), 7.41-7.37 (3H, m), 7.27-7.22 (2H, m), 7.17 (1H, m), 6.83 (1H, dd, J=3.5, 1.5Hz), 6.49 (1H, d, J=16Hz), 6.35 (1H, dd, J=3.5, 1.5Hz), 5.02 (2H, s), 3.53 (2H, d, J=7.5 Hz), 1.74-1.50 (1H, m), 0.90 (6H, d, J=6.5Hz).

Example 18(95)

4-[2-(N-propyl-phenylsulfonylamino)-5-methylphenoxymethyl]cinnamic acid

[0305]

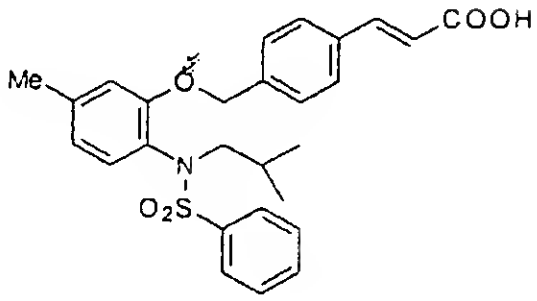


TLC : Rf 0 33 ($CHCl_3$: MeOH : AcOH= 100 : 5 : 1).
NMR : δ 7 79 (1H, d, J=16.0Hz), 7.67 (2H, m), 7.51 (2H, d, J=8.0Hz), 7.24-7.43 (3H, m), 7.17 (2H, d, J=8.0Hz), 7.15 (1H, d, J=8.0Hz), 6.78 (1H, m), 6.68 (1H, m), 6.47 (1H, d, J=16.0Hz), 4.79 (2H, brs), 3.55 (2H, m), 2.34 (3H, s), 1.47 (2H, m), 0.87 (3H, t, J=7.2Hz).

Example 18(96)

4-[2-(N-isobutyl-phenylsulfonylamino)-5-methylphenoxymethyl]cinnamic acid

[0306]

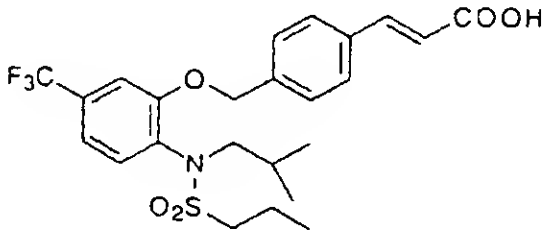


TLC : Rf 0.37 ($CHCl_3$: MeOH : AcOH= 100 : 5 : 1);
NMR : δ 7.79 (1H, d, J=16.0Hz), 7.63 (2H, m), 7.51 (2H, d, J=8.2Hz), 7.24-7.46 (3H, m), 7.18 (1H, d, J=7.8Hz), 7.16 (2H, d, J=8.2Hz), 6.78 (1H, m), 6.66 (1H, m), 6.48 (1H, d, J=16.0Hz), 4.74 (2H, m), 3.41 (2H, m), 2.33 (3H, s), 1.61 (1H, m), 0.89 (6H, d, J=6.4Hz).

Example 18(97)

4-[2-(N-isobutyl-propylsulfonylamino)-5-trifluoromethylphenoxymethyl]cinnamic acid

[0307]

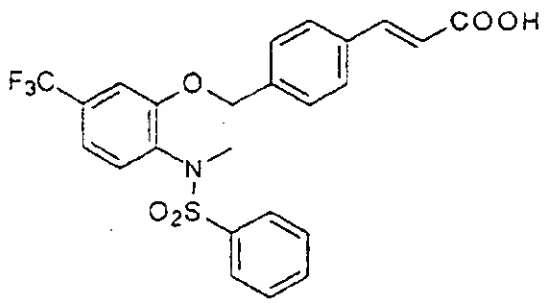


TLC : Rf 0.36 ($CHCl_3$: MeOH : AcOH= 100 : 5 : 1);
NMR : δ 7.80 (1H, d, J=16.0Hz), 7.62 (2H, d, J=8.4Hz), 7.44-7.56 (3H, m), 7.24-7.33 (2H, m), 6.50 (1H, d, J=16.0Hz), 5.17 (2H, s), 3.44 (2H, d, J=7.4Hz), 2.87 (2H, m), 7.15 (2H, m), 1.55 (1H, m), 0.90 (6H, d, J=6.6Hz), 0.83 (3H, t, J=7.4Hz).

Example 18(98)

4-[2-(N-methyl-phenylsulfonylamino)-5-trifluoromethylphenoxymethyl]cinnamic acid

[0308]

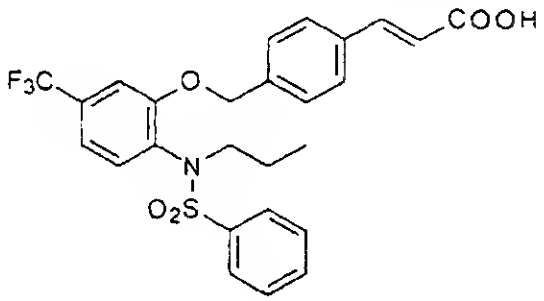


TLC : Rf 0.44 ($CHCl_3$: MeOH = 9 : 1);
NMR : δ 7.79 (1H, d, J=16.2Hz), 7.7-7.6 (2H, m), 7.6-7.2 (7H, m), 7.2-7.1 (3H, m), 6.49 (1H, d, J=16.2Hz), 4.88 (2H, s), 3.23 (3H, s).

Example 18(99)

4-[2-(N-propyl-phenylsulfonylamino)-5-trifluoromethylphenoxymethyl]cinnamic acid

[0309]

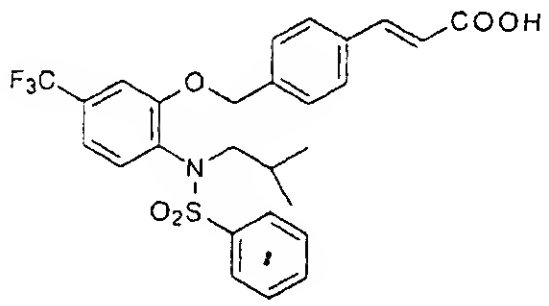


TLC : Rf 0.43 ($CHCl_3$: MeOH = 9 : 1);
NMR : δ 7.80 (1H, d, J=16.0Hz), 7.7-7.6 (2H, m), 7.6-7.1 (10H, m), 6.49 (1H, d, J=16.0Hz), 4.86 (2H, s), 3.57 (2H, t, J=7.2Hz), 1.6-1.3 (2H, m), 0.87 (3H, t, J=7.2Hz).

Example 18(100)

4-[2-(N-isobutyl-phenylsulfonylamino)-5-trifluorom thylphenoxymethyl]cinnamic acid

[0310]

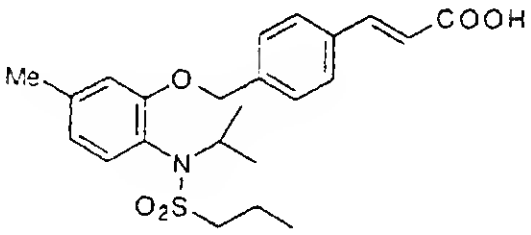


TLC : Rf 0.47 ($CHCl_3$: MeOH = 9 : 1);
NMR : δ 7.80 (1H, d, J=16.0Hz), 7.7-7.1 (12H, m), 6.49 (1H, d, J=16.0Hz), 4.9-4.7 (2H, br), 3.42 (2H, d, J=7.6Hz), 1.7-1.5 (1H, m), 0.89 (6H, d, J=6.6Hz).

Example 18(101)

4-[2-(N-isopropyl-propylsulfonylamino)-5-methylphenoxymethyl]cinnamic acid

[0311]

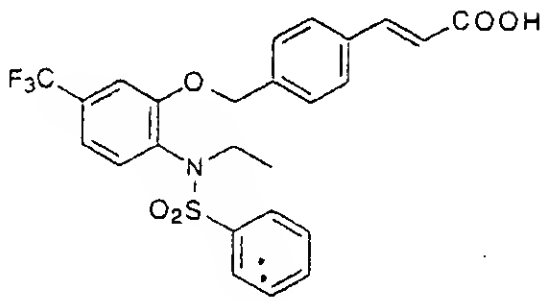


TLC : Rf 0.44 ($CHCl_3$: MeOH = 9 : 1).
NMR : δ 7.79 (1H, d, J=16.0Hz), 7.53 (4H, m), 7.14 (1H, m), 6.80 (2H, m), 6.47 (1H, d, J=16.0Hz), 5.07 (2H, s), 4.31 (1H, m), 2.94 (2H, m), 1.79 (2H, m), 1.23 (3H, d, J=6.6Hz), 1.08 (3H, d, J=6.6Hz), 0.83 (3H, t, J=7.2Hz).

Example 18(102)

4-[2-(N-ethyl-phenylsulfonylamino)-5-trifluoromethylphenoxymethyl]cinnamic acid

[0312]

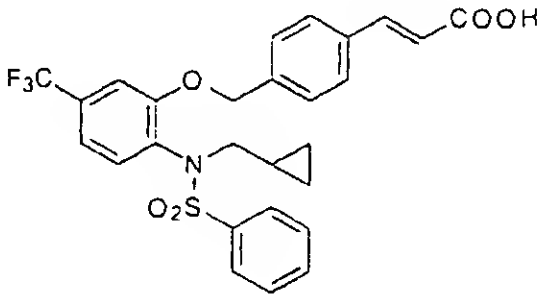


TLC : Rf 0.37 ($CHCl_3$: MeOH = 9 : 1);
NMR : δ 7.79 (1H, d, J=16.0Hz), 7.60-7.71 (2H, m), 7.15-7.55 (10H, m), 6.49 (1H, d, J=16.0Hz), 4.89 (2H, s), 3.67 (2H, q, J=7.0Hz), 1.09 (3H, t, J=7.0Hz).

Example 18(103)

4-[2-(N-cyclopropylmethyl-phenylsulfonylamino)-5-trifluoromethylphenoxymethyl]cinnamic acid

[0313]

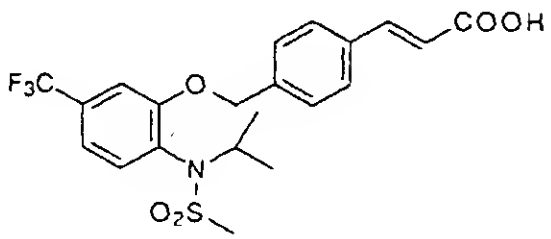


TLC : Rf 0.47 ($CHCl_3$: MeOH = 9 : 1);
NMR : δ 7.80 (1H, d, J=16.0Hz), 7.14-7.55 (10H, m), 7.67 (2H, m), 6.49 (1H, d, J=16.0Hz), 4.88 (2H, s), 3.49 (2H, d, J=7.0Hz), 0.87 (1H, m), 0.37 (2H, m), 0.06 (2H, m).

Example 18(104)

4-[2-(N-isopropyl-methylsulfonylamino)-5-trifluoromethylphenoxymethyl]cinnamic acid

[0314]

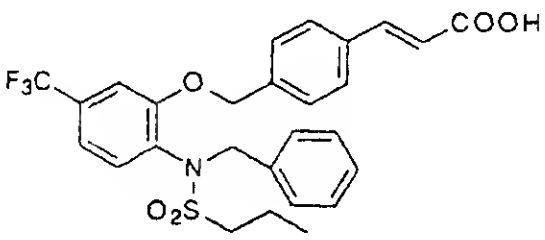


TLC : Rf 0.47 ($CHCl_3$: MeOH = 9 : 1);
NMR : δ 7.76 (1H, d, J=16.0Hz), 7.61 (2H, d, J=8.4Hz), 7.49 (2H, d, J=8.4Hz), 7.37 (3H, m), 6.48 (1H, d, J=16.0Hz), 5.14 (2H, s), 4.31 (1H, m), 2.89 (3H, s), 1.28 (3H, d, J=6.6Hz), 1.09 (3H, d, J=6.6Hz).

Example 18(105)

4-[2-(N-benzyl-propylsulfonylamino)-5-trifluoromethylphenoxymethyl]cinnamic acid

[0315]

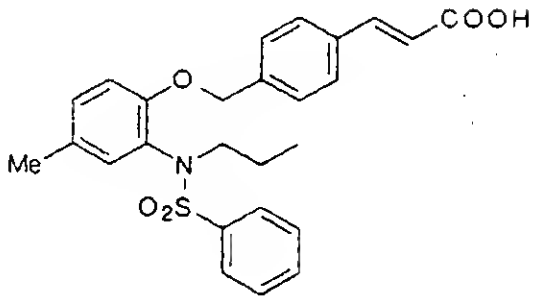


TLC : Rf 0.29 ($CHCl_3$: MeOH : AcOH = 100 : 5 : 1);
NMR : δ 7.82 (1H, d, J=16.2Hz), 7.65 (2H, d, J=8.4Hz), 7.51 (2H, d, J=8.4Hz), 7.09-7.31 (8H, m), 6.52 (1H, d, J=16.2Hz), 5.17 (2H, s), 4.78 (2H, s), 2.94 (2H, m), 1.80 (2H, m), 0.85 (2H, t, J=7.4Hz).

Example 18(106)

4-[2-(N-propyl-phenylsulfonylamino)-4-methylphenoxymethyl]cinnamic acid

[0316]

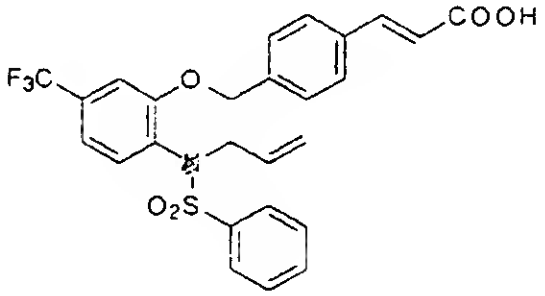


TLC : Rf 0.39 ($CHCl_3$: MeOH = 9 : 1);
NMR : δ 7.79 (1H, d, J=16.0Hz), 7.70-7.65 (2H, m), 7.50 (2H, d, J=8.0Hz), 7.42-7.38 (1H, m), 7.30 (2H, t, J=8.0Hz), 7.16 (2H, d, J=8.0Hz), 7.11 (1H, d, J=1.5Hz), 7.07 (1H, dd, J=1.5, 8.0Hz) , 6.74 (1H, d, J=8.0Hz), 6.47 (1H, d, J=16.0Hz), 4.90-4.70 (2H, br), 3.70-3.50 (2H, br), 2.29 (3H, s), 1.55-1.45 (2H, m), 0.88 (3H, t, J=7.0Hz).

Example 18(107)

4-[2-[N-(prop-2-enyl)-phenylsulfonylamino]-5-trifluoromethylphenoxymethyl]cinnamic acid

[0317]

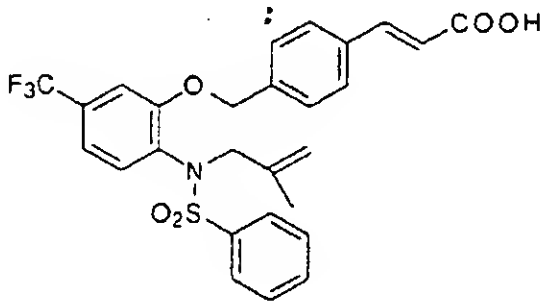


TLC : Rf 0.35 ($CHCl_3$: MeOH = 9 : 1);
NMR : δ 7.80 (1H, d, J=16.0Hz), 7.71-7.68 (2H, m), 7.54 (2H, d, J=8.0Hz), 7.49-7.45 (1H, m), 7.40 (1H, d, J=8.0Hz), 7.38-7.33 (2H, m), 7.25 (1H, dd, J=2.0, 8.0Hz), 7.19 (2H, d, J=8.0Hz), 7 .12 (1H, d, J=2.0Hz), 6.49 (1H, d, J=16.0Hz), 5.80-5.70 (1H, m), 5.07-5.02 (2H, m), 4.88 (2H, s), 4.5-4.3 (2H, m).

Example 18(108)

4-[2-[N-(2-methylprop-2-enyl)-phenylsulfonylamino]-5-trifluoromethylphenoxymethyl]cinnamic acid

[0318]

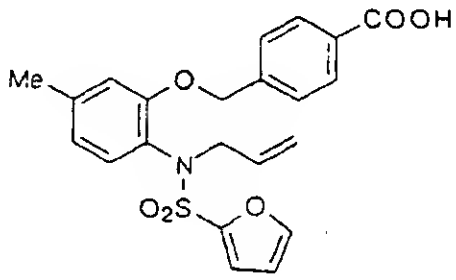


TLC : Rf 0.39 ($CHCl_3$: MeOH = 9 : 1);
NMR : δ 7.80 (1H, d, J=16.0Hz), 7.68-7.63 (2H, m), 7.54 (2H, d, J=8.0Hz), 7.48-7.44 (1H, m), 7.41 (1H, d, J=8.0Hz), 7.35 (2H, t, J=8.0Hz), 7.25 (1H, dd, J=1.5, 8.0Hz), 7.17 (2H, d, J=8.0Hz), 7.10 (1H, d, J=1.5Hz), 6.50 (1H, d, J=16.0Hz), 4.84 (2H, s), 4.73 (1H, s), 4.68 (1H, s), 4.20 (2H, s), 1.74 (3H, s).

Example 18(109)

4-[2-[N-(prop-2-enyl)-2-furanylsulfonylamino]-5-methylphenoxymethyl]benzoic acid

[0319]

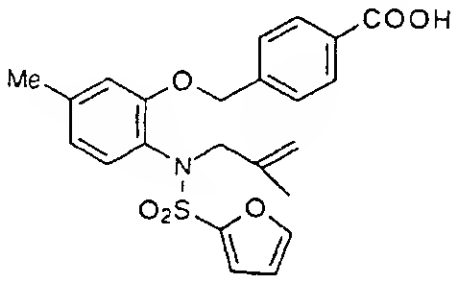


TLC : Rf 0.21 (hexane : AcOEt = 1 : 1);
NMR : δ 8.14-8.13 (2H, m), 7.45 (2H, d, J=8.5Hz), 7.28 (1H, m), 7.10 (1H, d, J=7.5Hz), 6.85 (1H, m), 6.84-6.76 (1H, m), 6.71 (1H, s), 6.34 (1H, m), 5.88-5.79 (1H, m), 5.11-5.02 (4H, m), 4.33 (2H, bs), 2.32 (3H, bs).

Example 18(110)

4-[2-[N-(2-methylprop-2-enyl)-2-furanylsulfonylamino]-5-methylphenoxymethyl]benzoic acid

[0320]

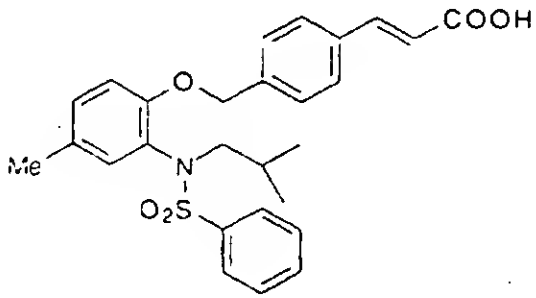


TLC : Rf 0.24 (hexane : AcOEt = 1 : 1);
NMR : δ 8.14-8.13 (2H, m), 7.44 (2H, d, J=8Hz), 7.26 (1H, m), 7.13 (1H, d, J=8Hz), 6.82 (1H, m), 6.78-6.69 (1H, m), 6.69 (1H, s), 6.33 (1H, m), 5.00 (2H, s), 4.76 (1H, dd, J=9.5, 1.5 Hz), 4.30 (2H, bs), 2.32 (3H, s), 1.78 (3H, s).

Example 18(111)

4-[2-(N-isobutyl-phenylsulfonylamino)-4-methylphenoxymethyl]cinnamic acid

[0321]

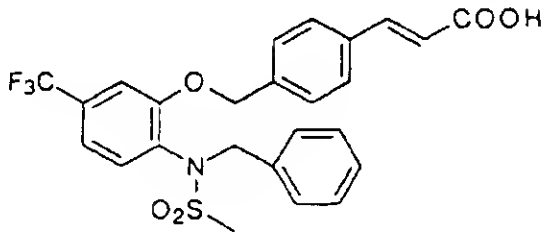


TLC : Rf 0.37 ($CHCl_3$: MeOH = 9 . 1).
NMR . δ 7.79 (1H, d, J=16.0Hz), 7.70-7.60 (2H, m), 7.50 (2H, d, J=8.0Hz), 7.40-7.35 (1H, m), 7.30-7.20 (2H, m), 7.20-7.10 (3H, m), 7.05 (1H, dd, J=2.0, 8.0Hz), 6.72 (1H, d, J=8.0Hz), 6.47 (1H, d, J=16.0Hz), 4.9-4.5 (2H, m), 3.5-3.3 (2H, m), 2.29 (3H, s), 1.7-1.6 (1H, m), 1.0-0.8 (6H, m).

Example 18(112)

4-[2-(N-benzyl-methylsulfonylamino)-5-trifluoromethylphenoxymethyl]cinnamic acid

[0322]

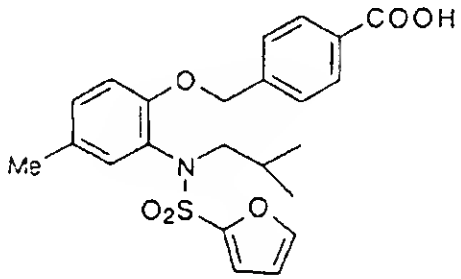


TLC : Rf 0.62 ($CHCl_3$: MeOH = 9 : 1);
NMR : δ 7.80 (1H, d, J=16.0Hz), 7.64 (2H, d, J=8.4Hz), 7.48 (2H, d, J=8.4Hz), 7.24 (8H, m), 6.50 (1H, d, J=16.0Hz), 5.18 (2H, s), 4.77 (2H, s), 2.88 (3H, s).

Example 18(113)

4-[2-(N-isobutyl-2-furanylsulfonylamino)-4-methylphenoxymethyl]benzoic acid

[0323]

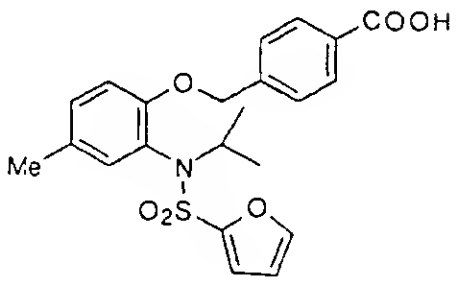


TLC : Rf 0.26 (AcOEt : hexane = 1 : 1);
NMR : δ 8.11 (2H, d, J=8Hz), 7.41 (2H, d, J=8Hz), 7.25 (1H, m), 7.09 (1H, d, J=2Hz), 7.06 (1H, dt, J=8,2Hz), 6.80 (1H, dd, J=4, 1Hz), 6.76 (1H, d, J=8Hz), 6.31 (1H, dd, J=2, 2Hz), 5.20-4.80 (2H, brs), 3.53 (2H, brs), 2.28 (3H, s), 1.67 (1H, m), 0.92 (6H, brs).

Example 18(114)

4-[2-(N-isopropyl-2-furanylsulfonylamino)-4-methylphenoxymethyl]benzoic acid

[0324]

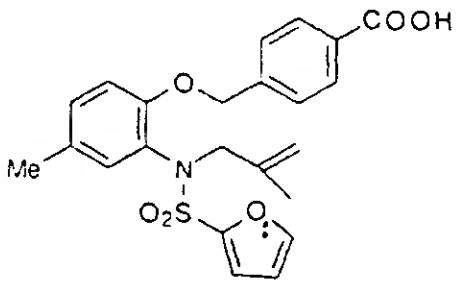


TLC : Rf 0.19 (AcOEt : hexane = 1 : 1);
NMR : δ 8.12 (2H, d, J=8Hz), 7.55 (2H, d, J=8Hz), 7.44 (1H, d, J=2Hz), 7.11 (1H, dd, J=8, 2Hz), 6.91 (1H, dd, J=3, 1Hz), 6.87 (1H, d, J=3Hz), 6.84 (1H, d, J=8Hz), 6.42 (1H, dd, J=3, 1Hz), 5.10 (2H, s), 4.48 (1H, m), 2.27 (3H, s), 1.12 (6H, d, J=7Hz).

Example 18(115)

4-[2-[N-(2-methylprop-2-enyl)-2-furanylsulfonylamino]-4-methylphenoxymethyl]benzoic acid

[0325]

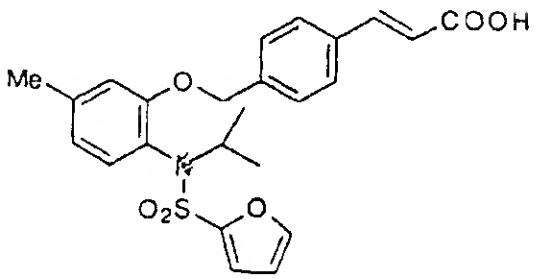


TLC : Rf 0.21 (AcOEt : hexane = 1 : 1).
NMR : δ 8.12 (2H, d, J=8Hz), 7.42 (2H, d, J=8Hz), 7.26 (1H, m), 7.07 (1H, d, J=2Hz), 7.06 (1H, dd, J=8, 2Hz), 6.83 (1H, d, J=3Hz), 6.75 (1H, d, J=8Hz), 6.33 (1H, dd, J=3, 2Hz), 4.97 (2H, s), 4.77 (2H, s), 4.30 (2H, s), 2.28 (3H, s), 1.79 (3H, s).

Example 18(116)

4-[2-(N-isopropyl-2-furanylsulfonylamino)-5-methylphenoxymethyl]cinnamic acid

[0326]

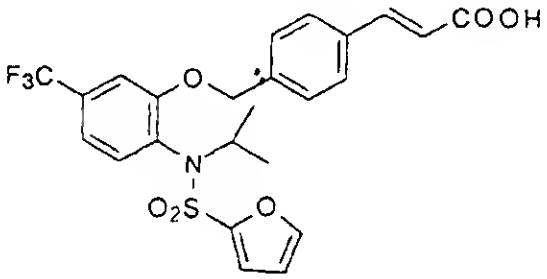


TLC : Rf 0.20 (hexane : AcOEt = 1 : 1);
NMR: δ 7.80 (1H, d, J=16Hz), 7.61-7.45 (4H,m), 7.43 (1H, m), 6.93-6.88 (2H, m), 6.79-6.73 (2H, m), 6.47 (1H, d, J=16Hz), 6.41 (1H, dd, J=3.5, 2Hz), 5.07 (2H, s), 4.56-4.43 (1H, m), 2.34 (3H, s), 1.10 (6H, dd, J=6.5, 4Hz).

Example 18(117)

4-[2-(N-isopropyl-2-furanylsulfonylamino)-5-trifluoromethylphenoxymethyl]cinnamic acid

[0327]

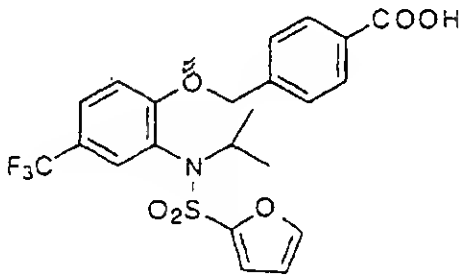


TLC : Rf 0.18 (hexane : AcOEt = 1 : 1);
NMR : δ 7.80 (1H, d, J=16Hz), 7.63-7.51 (4H, m), 7.46 (1H, dd, J=1.5, 1Hz), 7.23-7.20 (3H, m), 6.94 (1H, dd, J=3.5, 1Hz), 6.52-6.43 (3H, m), 5.14 (2H, s), 4.51-4.41 (1H, m), 1.09 (6H, dd, J=6.5, 1Hz).

Example 18(118)

4-[2-(N-isopropyl-2-furanylsulfonylamino)-4-trifluoromethylphenoxymethyl]benzoic acid

[0328]

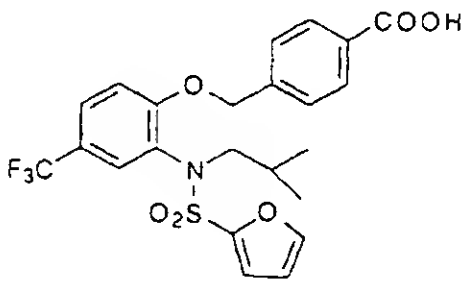


TLC : Rf 0.35 (AcOEt : hexane : AcOH= 50 : 50 : 1);
NMR : δ 8.16 (2H, d, J=8.5Hz), 7.60 (3H, m), 7.38 (1H, dd, J=1.0, 2.0Hz), 7.26 (1H, m), 7.05 (1H, d, J=9.0Hz), 6.95 (1H, d, J=3.0Hz), 6.47 (1H, dd, J=2.0, 3.5Hz), 5.22 (2H, s), 4.52 (1H, sept, J=7.0Hz), 1.12 (3H, d, J=7.0Hz), 1.10 (3H, d, J=7.0Hz).

Example 18(119)

4-[2-(N-isobutyl-2-furanylsulfonylamino)-4-trifluoromethylphenoxymethyl]benzoic acid

[0329]

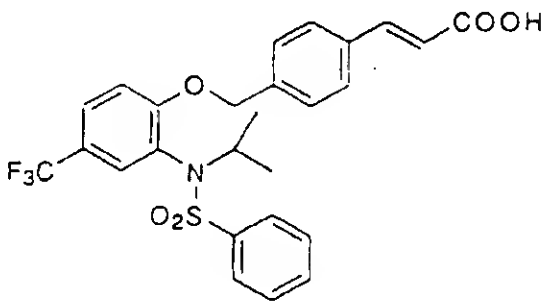


TLC . Rf 0.35 (AcOEt : hexane : AcOH= 50 : 50 . 1);
NMR δ 8.15 (2H, d, J=9.0Hz), 7.55 (1H, m), 7.48 (2H, d, J=9.0Hz), 7.44 (1H, d, J=2.0Hz), 7.35 (1H, dd, J=1.0, 2.0Hz), 6 99 (1H, d, J=9.0Hz), 6.86 (1H, dd, J=1.0, 2.0Hz), 6.39 (1H, dd, J=2.0, 4.0Hz), 5.12 (2H, br), 3.52 (2H, d, J=7.0Hz), 1.64 (1H, m), 0.92 (6H, d, J=6.5Hz).

Example 18(120)

4-[2-(N-isopropyl-phenylsulfonylamino)-4-trifluoromethylphenoxymethyl]cinnamic acid

[0330]

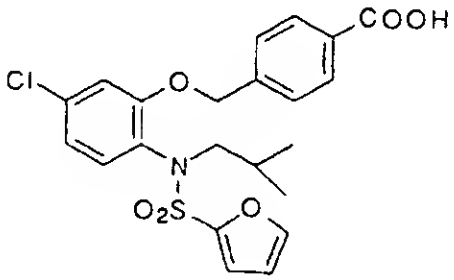


TLC · Rf 0.35 (AcOEt : hexane : AcOH= 50 · 50 · 1);
NMR : δ 7.81 (3H, m), 7.58-7.62 (3H, m), 7.53 (1H, m), 7.49 (2H, d, J=8.0Hz), 7.41 (2H, m), 7.24 (1H, d,J=2.0Hz), 7.07 (1H, d, J=8.5Hz), 6.49 (1H, d, J=16.5Hz), 5.13 (1H, d, J=12.5Hz), 5.12 (1H, d, J=12.5Hz), 4.40 (1H, sept, J=6.5Hz), 4.07 (3H, d, J=6.5Hz), 1.02 (3H, d, J=6.5Hz).

Example 18(121)

4-[2-(N-isobutyl-2-furanylsulfonylamino)-5-chlorophenoxymethyl]benzoic acid

[0331]

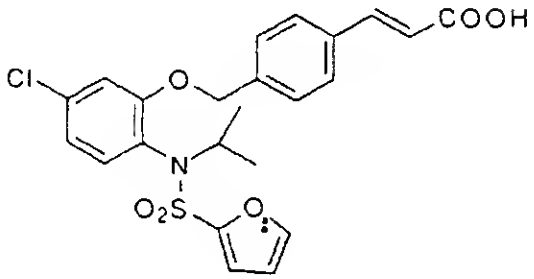


TLC · Rf 0.36 (AcOEt : hexane · AcOH= 50 · 50 · 1);
NMR : δ 8.14 (2H, d, J=8.5Hz), 7.44 (2H, d, J=8.5Hz), 7.26 (1H, m), 7.21 (1H, d, J=9.0Hz), 6.98 (1H, dd, J=2.5, 8.0Hz), 6.91 (1H, d, J=2.5Hz), 6.82 (1H, d, J=4.5Hz), 6.34 (1H, d, J=2.0, 3.0Hz), 5.00 (2H, br), 3.51 (2H, brs), 1.65 (1H, m), 0 91 (6H, d, J=6.5Hz).

Example 18(122)

4-[2-(N-isopropyl-2-furanylsulfonylamino)-5-chlorophenoxymethyl]cinnamic acid

[0332]

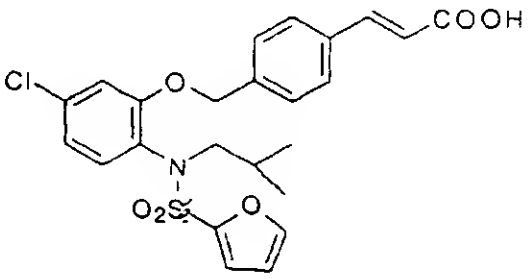


TLC : Rf 0.49 ($CHCl_3$: MeOH = 9 : 1);
NMR : δ 7.80 (1H, d, J=16.2Hz), 7.60 (2H, d, J=8.4Hz), 7.50 (2H, d, J=8.4Hz), 7.45-7.42 (1H, m), 7.02-6.90 (4H, m), 6.53-6.40 (2H, m), 5.07 (2H, s), 4.60-4.40 (1H, m), 1.10 (3H, d, J=6.6Hz), 1.07 (3H, d, J=6.6Hz).

Example 18(123)

4-[2-(N-isobutyl-2-furanylsulfonylamino)-5-chlorophenoxymethyl]cinnamic acid

[0333]

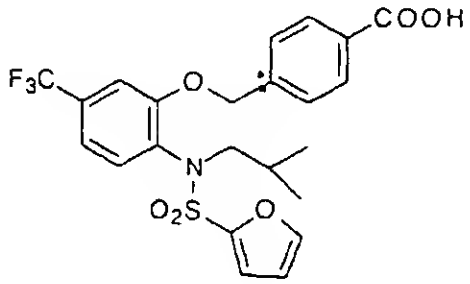


TLC : Rf 0.49 ($CHCl_3$: MeOH = 9 . 1),
NMR . δ 7.80 (1H, d, J=15.8Hz), 7.58 (2H, d, J=8.0Hz), 7.37 (2H, d, J=8.0Hz), 7.25 (1H, dd, J=1.0, 1.8Hz), 7.20 (1H, d, J=8.2Hz), 7 00-6.90 (2H, m), 6.81 (1H, dd, J=1 0, 3.6Hz), 6.49 (1H, d, J=15.8Hz), 6.33 (1H, dd, J=1.8, 3.6Hz), 4.95 (2H, s), 3.60-3.40 (2H, m), 1.80-1.50 (1H, m), 0.90 (6H, d, J=6.6Hz).

Example 18(124)

4-[2-(N-isobutyl-2-furanylsulfonylamino)-5-trifluoromethylphenoxymethyl]benzoic acid

[0334]

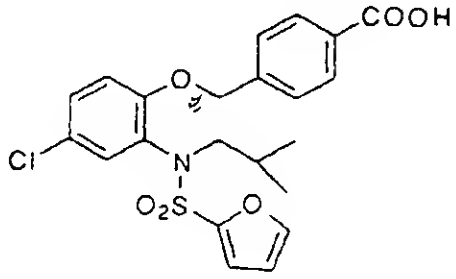


TLC : Rf 0.20 (hexane : AcOEt = 1 : 1);
NMR : δ 8.18-8.14 (2H, m), 7.48-7.40 (2H, m), 7.30-7.26 (2H, m), 7.16 (1H, m), 6.84 (1H, dd, J=3.5,1 Hz), 6.35 (1H, dd, J=3.5, 2Hz), 5.07 (2H, s), 3.54 (2H, d, J=7Hz), 1.64 (1H, sept., J=7Hz), 0.90 (6H, d, J=7Hz).

Example 18(125)

4-[2-(N-isobutyl-2-furanylsulfonylamino)-4-chlorophenoxymethyl]benzoic acid

[0335]

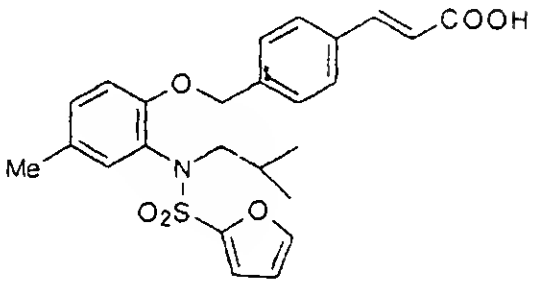


TLC : Rf 0.36 ($CHCl_3$: MeOH = 9 : 1),
NMR : δ 8.14 (2H, d, J=8.4Hz), 7.44 (2H, d, J=8.4Hz), 7.34-7.20 (3H, m), 6.90-6.80 (2H, m), 6.37 (1H, dd, J=1.8, 3.0Hz), 5.03 (2H, s), 3.51 (2H, d, J=7.2Hz), 1 80-1.50 (1H, m), 0.91 (6H, d, J=6.6Hz).

Example 18(126)

4-[2-(N-isobutyl-2-furanylsulfonylamino)-4-methylphenoxymethyl]cinnamic acid

[0336]

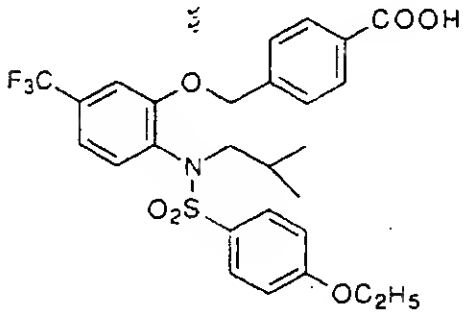


TLC : Rf 0.33 ($CHCl_3$: MeOH = 9 : 1);
NMR : δ 7.80 (1H, d, J=16.0Hz), 7.57 (2H, d, J=8.0Hz), 7.36 (2H, d, J=8.0Hz), 7.28-7.22 (1H, m), 7.12-7.02 (2H, m), 6.84-6.74 (2H, m), 6.48 (1H, d, J=16.0Hz), 6.32 (1H, ddt J=1.8, 3.6Hz), 4.92 (2H, s), 3.54 (2H, d, J=7.0Hz), 2.28 (3H, s), 1.80-1.60 (1H, m), 0.92 (6H, d, J=6.6Hz).

Example 18(127)

4-[2-(N-isobutyl-4-ethoxyphenylsulfonylamino)-5-trifluoromethylphenoxymethyl]benzoic acid

[0337]

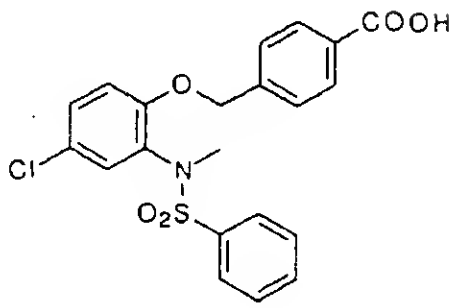


TLC : Rf 0.35 ($CHCl_3$: MeOH : AcOH= 100 : 5 : 1);
NMR : δ 8.09 (2H, d, J=8.5Hz), 7.52 (2H, d, J=8.5Hz), 7.46 (1H, d, J=8.5Hz), 7.25-7.29 (3H, m), 7.13 (1H, brd, J=1.5Hz), 6.73 (2H, d, J=9.0Hz), 4.92 (2H, br), 3.96 (2H, q, J=7.5Hz), 3.40 (2H, brs), 1.59 (1H, m), 1.42 (3H, t, J=7.5Hz), 0.90 (6H, brd, J=6.0Hz).

Example 18(128)

4-[2-(N-methyl-phenylsulfonylamino)-4-chlorophenoxymethyl]benzoic acid

[0338]

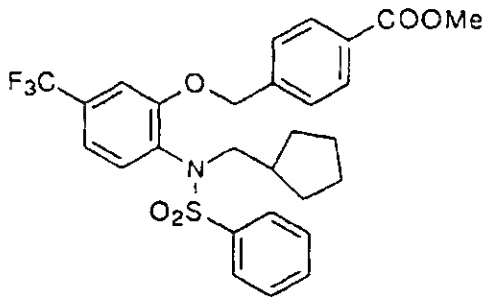


TLC : Rf 0.43 ($CHCl_3$: MeOH : H_2O = 9 : 1 : 0.1);
NMR ($DMSO-d_6$) : δ 7.88 (2H, d, J=8.6Hz), 7.66-7.38 (6H, m), 7.25-7.11 (4H, m), 4.95 (2H, s), 3.15 (3H, s).

Example 19

Methyl 4-[2-(N-cycopentymethyl-phenysulfonylamino)-5-trifluoromethylphenoxymethyl]benzoate

[0339]



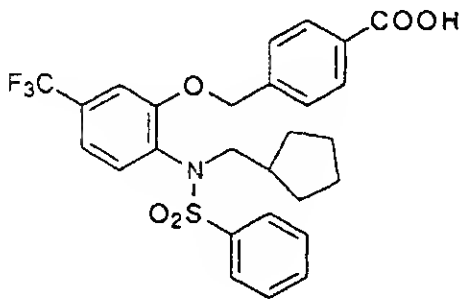
[0340] To a solution of methyl 4-(2-phenylsulfonylamino-5-trifluoromethylphenoxymethyl)benzoate (251 mg, prepared in Example 15.), triphenylphosphine (142 mg) and cyclopentylmethanol (54 mg) in THF (2 ml), diethyl azodicarboxylate (89 ml; abbreviated as DEAD.) was added at 0°C. The mixture was stirred overnight at room temperature. The reaction solution was purified on silica gel chromatography (hexane : AcOEt = 7 : 1) to give the title compound (333 mg) having the following physical data.

TLC : Rf 0.51 (hexane : AcOEt = 3 : 1);
NMR : δ 8.01 (2H, d, J=8.4Hz), 7.63-7.58 (2H, m), 7.48-7.25 (5H, m), 7.17 (2H, d, J=8.4Hz), 7.09 (1H, d, J=1.4Hz), 4.83 (2H, br), 3.95 (3H, s), 3.55 (2H, d-like), 1.92-1.09 (9H, m).

Example 20

4-[2-(N-cyclopentylmethyl-phenylsulfonylamino)-5-trifluoromethylphenoxymethyl]benzoic acid

[0341]



[0342] By using methyl 4-[2-(N-cyclopentylmethyl-phenylsulfonylamino)-5-trifluoromethylphenoxymethyl]benzoate (prepared in Example 19.), the title compounds having the following physicel data was obtained by the seme procedure as Example 2.

TLC : Rf 0.40 ($CHCl_3$: MeOH : H_2O = 9 : 1 : 0.1);
NMR : δ 8.09 (2H, d, J=8.2Hz), 7.65-7.61 (2H, m), 7.47-7.20 (7H, m), 7.11 (1H, d, J=1.8Hz), 4.89 (2H, br), 3.59-3.51 (2H, m), 1.93-1.10 (9H, m).

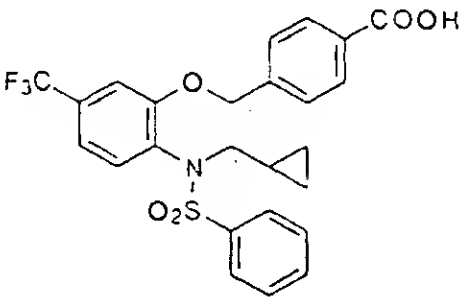
Example 20(1)-20(30)

[0343] By using the corresponding compounds, the title compounds having the following physical data were obtained by the same procedure as Reference Example 6→Reference Example 7→Example 7→Example 19→Example 2 or Reference Example 8→Reference Example 9→Reference Exemple 10→Example 9→Example 19→Example 2.

Example 20(1)

4-[2-(N-cyclopropylmethyl-phenylsulfonylamino)-5-trifluoromethylphenoxymethyl]benzoic acid

[0344]



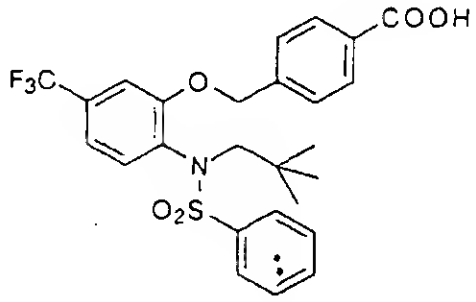
TLC : Rf 0.43 ($CHCl_3$: MeOH : H_2O = 9 . 1 : 0.1);
NMR : δ 8.09 (2H, d, J=8.2Hz), 7.70-7.65 (2H, m), 7.54-7.22 (7H, m), 7.14 (1H, d, J=1.8Hz), 4.93 (2H, s), 3.51 (2H,

d, J=7.2Hz), 0.96-0.81 (1H, m), 0.44-0.35 (2H, m), 0.10-0.02 (2H, m).

Example 20(2)

4-[2-(N-t-butylmethyl-phenylsulfonylamino)-5-trifluoromethylphenoxymethyl]benzoic acid

[0345]

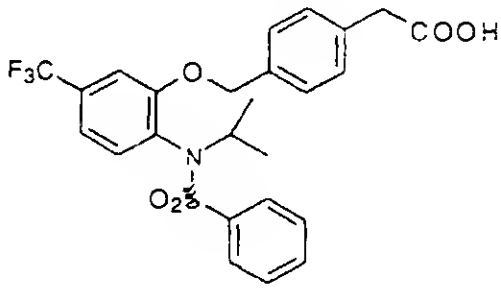


TLC : Rf 0.5 ($CHCl_3$: MeOH = 9 : 1);
NMR : δ 8.12 (2H, d, J=8.0Hz), 7.6-7.4 (4H, m), 7.4-7.2 (5H, m), 7.09 (1H, d, J=1.8Hz), 5.02 (1H, d, J=12.4Hz), 4.72 (1H, d, J=12.4Hz), 3.53 (2H, s), 0.86 (9H, s).

Example 20(3)

4-[2-(N-isopropyl-phenylsulfonylamino)-5-trifluoromethylphenoxymethyl]phenylacetic acid

[0346]

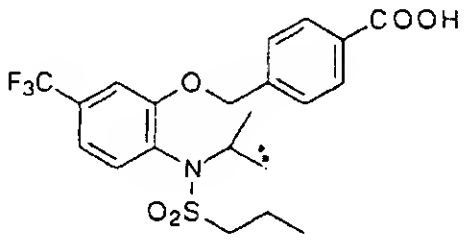


TLC Rf 0.47 ($CHCl_3$: MeOH : AcOH= 100 : 5 : 1);
NMR : δ 7.79 (2H, d, J=7.6Hz), 7.20-7.50 (10H, m), 5.01 (2H, s), 4.28 (1H, sept, J=6.6Hz), 3.71 (2H, s), 1.08 (3H, d, J=6.6Hz), 1.01 (3H, d, J=6.6Hz).

Example 20(4)

4-[2-(N-isopropyl-propylsulfonylamino)-5-trifluoromethylphenoxymethyl]benzoic acid

[0347]

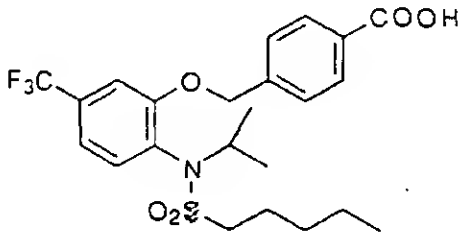


TLC : Rf 0.33 ($CHCl_3$: MeOH = 20 : 1);
NMR (CD_3Cl) : δ 8.13 (2H, d, J=8.0Hz), 7.54 (2H, d, J=8.0Hz), 7.30-7.46 (3H, m), 5.19 (2H, s), 4.32 (1H, sept, J=6.2Hz), 2.96 (2H, m), 1.78 (2H, m), 1.27 (2H, d, J=6.4Hz), 1.12 (2H, d, J=6.4Hz), 0.85 (3H, t, J=7.4Hz).

Example 20(5)

4-[2-(N-isopropyl-pentylsulfonylamino)-5-trifluoromethylphenoxymethyl]benzoic acid

[0348]

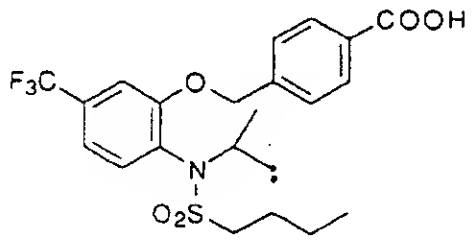


TLC: Rf 0.40 ($CHCl_3$: MeOH = 20 . 1);
NMR (CD_3Cl) : δ 8 17 (2H, d, J=8 4Hz), 7.59 (2H, d, J=8.4Hz), 7.12-7.41 (3H, m), 5.18 (2H, s), 4.32 (1H, sept, J=6.6Hz), 2.97 (2H, m), 1.74 (2H, m), 1 02-1.35 (8H, m), 0.82 (3H, t, J=6.8Hz).

Example 20(6)

4-[2-(N-isopropyl-butylsulfonylamino)-5-trifluoromethylphenoxymethyl]benzoic acid

[0349]

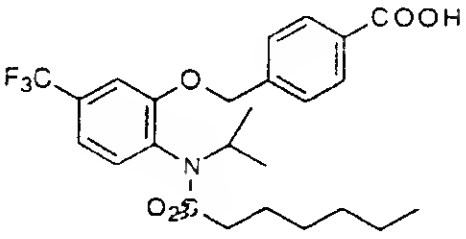


TLC : Rf 0.40 ($CHCl_3$: MeOH = 9 : 1);
NMR : δ 8.17 (2H, d, J=8.2Hz), 7.59 (2H, d, J=8.2Hz), 7.40 (1H, d, J=7.8Hz), 7.3-7.2 (2H, m), 5.18 (2H, s), 4.4-4.2 (1H, m), 3.1-2.9 (2H, m), 1.8-1.6 (2H, m), 1.4-1.0 (8H, m), 0.92 (3H, t, J=7.2Hz).

Example 20(7)

4-[2-(N-isopropyl-hexylsulfonylamino)-5-trifluoromethylphenoxymethyl]benzoic acid

[0350]

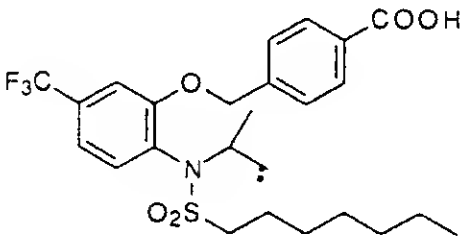


TLC : Rf 0.44 ($CHCl_3$: MeOH = 9 : 1);
NMR : δ 8.18 (2H, d, J=8.0Hz), 7.59 (2H, d, J=8.0Hz), 7.40 (1H, d, J=8.0Hz), 7.3-7.2 (2H, m), 5.18 (2H, s), 4.4-4.2 (1H, m), 3.0-2.9 (2H, m), 1.8-1.6 (2H, m), 1.3-1.0 (12H, m), 0.85 (3H, t, J=7.4Hz).

Example 20(8)

4-[2-(N-isopropyl-heptylsulfonylamino)-5-trifluoromethylphenoxymethyl]benzoic acid

[0351]

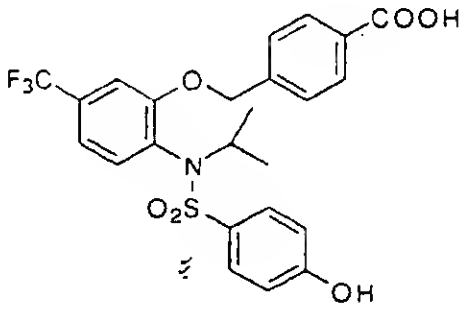


TLC : Rf 0.48 ($CHCl_3$: MeOH = 9 : 1);
NMR : δ 8.18 (2H, d, J=8.0Hz), 7.59 (2H, d, J=8.0Hz), 7.40 (1H, d, J=8.0Hz), 7.3-7.2 (2H, m), 5.18 (2H, s), 4.4-4.2 (1H, m), 3.0-2.9 (2H, m), 1.9-1.6 (2H, m), 1.4-1.0 (14H, m), 0.86 (3H, t, J=6.2Hz).

Example 20(9)

4-[2-(N-isopropyl-4-hydroxyphenylsulfonylamino)-5-trifluoromethylphenoxymethyl]benzoic acid

[0352]

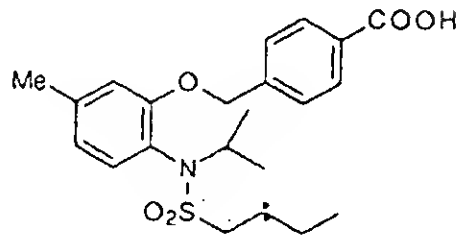


TLC : Rf 0.28 ($CHCl_3$: MeOH = 9 : 1);
NMR : δ 8.13 (2H, d, J=8.2Hz), 7.66 (2H, d, J=9.2Hz), 7.50 (2H, d, J=8.2Hz), 7.3-7.2 (3H, m), 6.72 (2H, d, J=9.2Hz), 5.10 (2H, s), 4.4-4.2 (1H, m), 3.0-1.5 (2H, br), 1.10 (3H, d, J=6.6Hz), 1.03 (3H, d, J=6.6Hz).

Example 20(10)

4-[2-(N-isopropyl-butylsulfonylamino)-5-methylphenoxymethyl]benzoic acid

[0353]

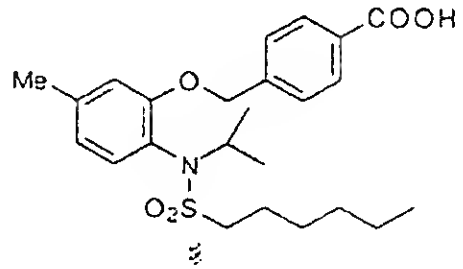


TLC : Rf 0.41 ($CHCl_3$: MeOH = 9 : 1);
NMR : δ 8.15 (2H, d, J=8.6Hz), 7.57 (2H, d, J=8.6Hz), 7.15 (1H, d, J=8.4Hz), 6.9-6.8 (2H, m), 5.13 (2H, s), 4.4-4.2 (1H, m), 3.1-2.9 (2H, m), 2.36 (3H, s), 1.8-1.6 (2H, m), 1.3-1.2 (5H, m), 1.10 (3H, d, J=6.6Hz), 0.81 (3H, t, J=7.4Hz).

Example 20(11)

4-[2-(N-isopropyl-hexylsulfonylamino)-5-methylphenoxymethyl]benzoic acid

[0354]

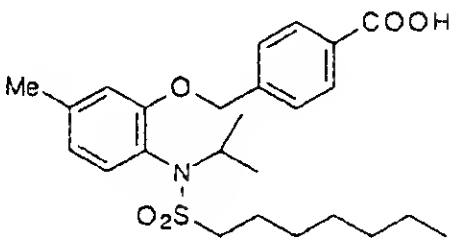


TLC : Rf 0.47 ($CHCl_3$: MeOH = 9 : 1);
NMR : δ 8.15 (2H, d, J=8.4Hz), 7.57 (2H, d, J=8.4Hz), 7.15 (1H, d, J=8.4Hz), 7.1-7.0 (2H, m), 5.13 (2H, s), 4.4-4.2 (1H, m), 3.0-2.9 (2H, m) 2.36 (3H, s), 1.8-1.6 (2H, m), 1.3-1.0 (12H, m), 0.84 (3H, t, J=6.4Hz).

Example 20(12)

4-[2-(N-isopropyl-heptylsulfonylamino)-5-methylphenoxymethyl]b nzoic acid

[0355]

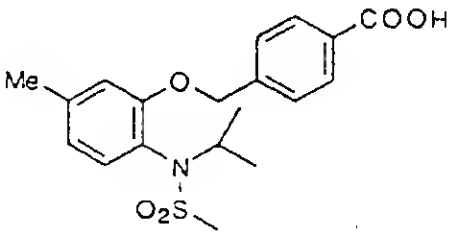


TLC : Rf 0.47 ($CHCl_3$: MeOH = 9 : 1);
NMR : δ 8.15 (2H, d, J=8.0Hz), 7.57 (2H, d, J=8.0Hz), 7.15 (1H, d, J=8.4Hz), 6.9-6.8 (2H, m), 5.13 (2H, s), 4.4-4.2 (1H, m), 3.0-2.9 (2H, m), 2.36 (3H, s), 1.9-1.6 (2H, m), 1.3-1.0 (14H, m), 0.85 (3H, t, J=6.2Hz).

Example 20(13)

4-[2-(N-isopropyl-methylsulfonylamino)-5-methylphenoxymethyl]benzoic acid

[0356]

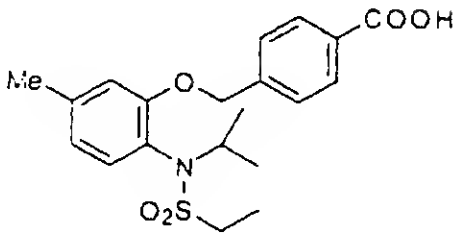


TLC : Rf 0.13 (hexane : AcOEt = 1 : 1),
NMR : δ 8.17-8.13 (2H, m), 7.58-7.53 (2H, m), 7.17-7.12 (1H, m), 6.8 (2H, m), 5.1 (2H, m), 4.33 (1H, sept., J=6.5Hz), 2.90 (3H, s), 2.36 (3H, s), 1.26 (3H, d, J=6.5Hz), 1.09 (3H, d, J=6.5Hz).

Example 20(14)

4-[2-(N-isopropyl-ethylsulfonylamino)-5-methylphenoxymethyl]benzoic acid

[0357]

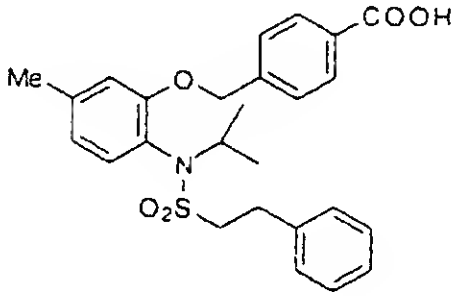


TLC : Rf 0.20 (hexane : AcOEt = 1 : 1);
NMR : δ 8.17-8.13 (2H, m), 7.59-7.55 (2H, m), 7.17-7.13 (1H, m), 6.8 (2H, m), 5.1 (2H, m), 4.33 (1H, sept., J=7Hz), 3.01 (2H, q, J=7Hz), 2.36 (3H, s), 1.29-1.20 (6H, m), 1.09 (3H, d, J=6.5Hz).

Example 20(15)

4-[2-(N-isopropyl-2-phenylethylsulfonylamino)-5-methylphenoxymethyl]benzoic acid

[0358]

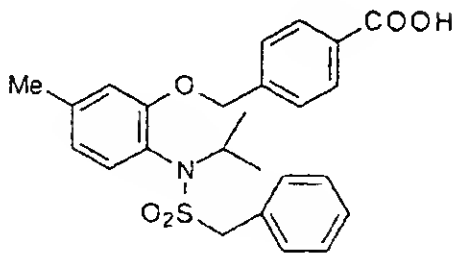


TLC : Rf 0.24 (hexane : AcOEt = 1 : 1);
NMR : δ 8.00-7.96 (2H, m), 7.44-7.40 (2H, m), 7.26-7.14 (4H, m), 7.05-7.01 (2H, m), 6.85-6.81 (2H, m), 5.07 (2H, s), 4.42-4.27 (1H, m), 3.4-3.2 (2H, m), 3.2-3.0 (2H, m), 2.36 (3H, s), 1.25 (3H, d, J=6.5Hz), 1.09 (3H, d, J=6.5Hz).

Example 20(16)

4-[2-(N-isopropyl-benzylsulfonylamino)-5-methylphenoxymethyl]benzoic acid

[0359]

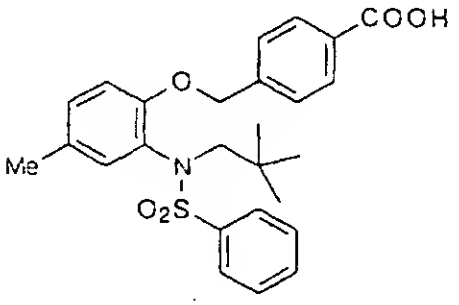


TLC : Rf 0.22 (hexane : AcOEt = 1 : 1);
NMR : δ 8.15-8.11 (2H, m), 7.63-7.59 (2H, m), 7.3 (2H, m), 6.92-6.88 (1H, m), 6.81-6.70 (2H, m), 5.2 (2H, m), 4.29 (2H, s), 4.18-4.02 (1H, m), 2.35 (3H, s), 1.12 (3H, d, J=6.5Hz), 1.04 (3H, d, J=6.5Hz).

Example 20(17)

4-[2-(N-t-butylmethyl-phenylsulfonylamino)-4-methylphenoxymethyl]benzoic acid

[0360]

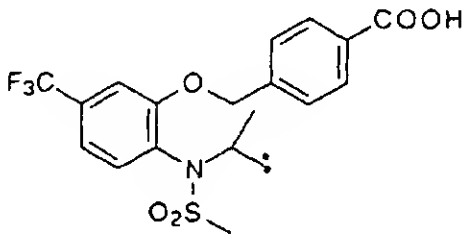


TLC : Rf 0.37 ($CHCl_3$: MeOH = 9 : 1);
NMR : δ 8.08 (2H, d, J=8Hz), 7.55 (2H, m), 7.39 (1H, m), 7.32-7.20 (4H, m), 7.17 (1H, d, J=2Hz), 7.03 (1H, dd, J=8 and 2Hz), 6.68 (1H, d, J=8Hz), 4.90 (1H, d, J=13Hz), 4.59 (1H, d, J=13Hz), 3.57 (1H, d, J=14Hz), 3.50 (1H, d, J=14Hz), 2.28 (3H, s), 0.88 (9H, s).

Example 20(18)

4-[2-(N-isopropyl-methylsulfonylamino)-5-trifluoromethylphenoxymethyl]benzoic acid

[0361]

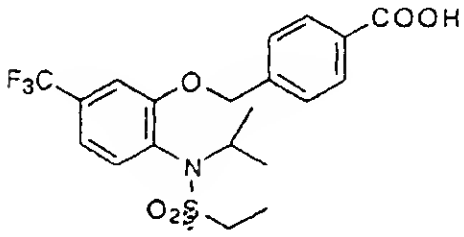


TLC : Rf 0.32 ($CHCl_3$: MeOH = 9 : 1);
NMR : δ 8.17 (2H, d, J=8.5Hz), 7.58 (2H, d, J=8.5Hz), , 7.43-7.23 (3H, m), 5.20 (2H, s), 4.32 (1H, m), 2.91 (3H, s), 1.29 (3H, d, J=7Hz), 1.10 (3H, d, J=7Hz).

Example 20(19)

4-[2-(N-isopropyl-ethylsulfonylamino)-5-trifluoromethylphenoxymethyl]benzoic acid

[0362]

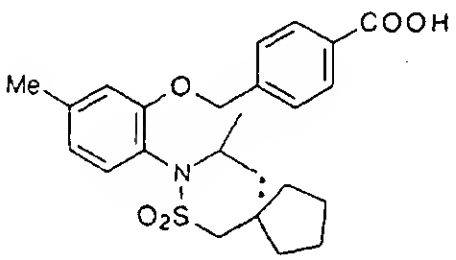


TLC : Rf 0.36 ($CHCl_3$: MeOH = 9 : 1);
NMR : δ 8 18 (2H, d, J=8.5Hz), 7.59 (2H, d, J=8.5Hz), , 7.43-7.23 (3H, m), 5.19 (2H, s), 4.33 (1H, m), 3.03 (2H, q, J= 7.5Hz), 1.32-1.17 (6H, m), 1.09 (3H, d, J=7Hz).

Example 20(20)

4-[2-(N-isopropyl-cyclopentylmethylsulfonylamino)-5-methylphenoxymethyl]benzoic acid

[0363]

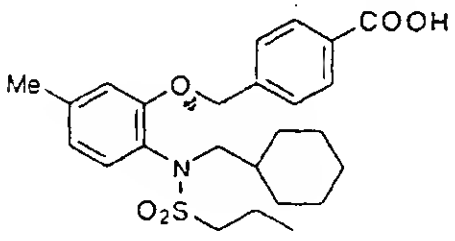


TLC : Rf 0.26 (hexane : AcOEt = 1 : 1);
NMR : δ 8.17-8.13 (2H, m), 7.59-7.55 (2H, m), 7.16-7.12 (1H, m), 6.83-6.80 (2H, m), 5.13 (2H, s), 4.31 (1H, sept., J=7Hz), 3.04-3.00 (2H, m), 2.36 (3H, s), 2.4-2.2 (1H, m), 2.0-1.8 (2H, m), 1.6-1.4 (4H, m), 1.24 (3H, d, J=7Hz), 1.3-1.1 (2H, m), 1.09 (3H, d, J=7Hz).

Example 20(21)

4-[2-(N-cyclohexylmethyl-propylsulfonylamino)-5-methylphenoxymethyl]benzoic acid

[0364]

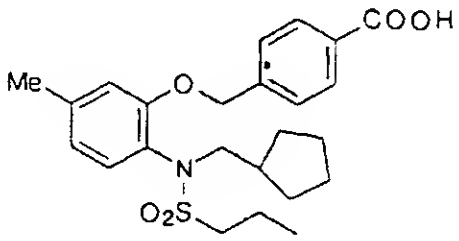


TLC : Rf 0.43 ($CHCl_3$: MeOH = 9 : 1);
NMR : δ 8.16 (2H, d, J=8.6Hz), 7.54 (2H, d, J=8.6Hz), 7.26 (1H, d, J=8.6Hz), 6.9-6.8 (2H, m), 5.17 (2H, s), 3.5-3.4 (2H, m), 2.9-2.8 (2H, m), 2.35 (3H, s), 2.0-1.0 (13H, m), 0.84 (3H, t, J=8.0Hz), 4.0-1.0 (1H, br).

Example 20(22)

4-[2-(N-cyclopentylmethyl-propylsulfonylamino)-5-methylphenoxymethyl]benzoic acid

[0365]

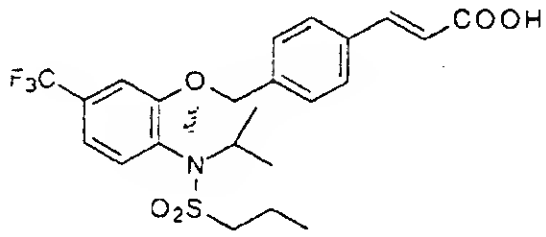


TLC : Rf 0.38 ($CHCl_3$: MeOH = 9 : 1);
NMR : δ 8.16 (2H, d, J=8.4Hz), 7.54 (2H, d, J=8.4Hz), 7.26 (1H, d, J=8.4Hz), 6.9-6.8 (2H, m), 5.17 (2H, s), 3.6-3.5 (2H, m), 2.9-2.8 (2H, m), 2.35 (3H, s), 2.0-1.0 (11H, m), 0.84 (3H, t, J=7.6Hz), 6.0-4.0 (1H, br).

Example 20(23)

4-[2-(N-isopropyl-propylsulfonylamino)-5-trifluoromethylphenoxymethyl]cinnamic acid

[0366]

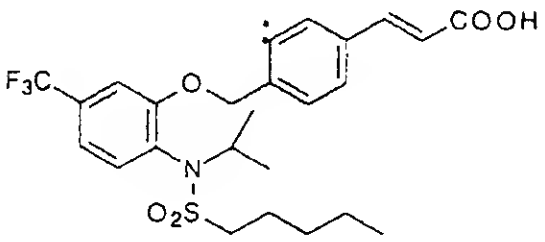


TLC : Rf 0.32 ($CHCl_3$: MeOH : AcOH= 100 : 5 : 1);
NMR : δ 7.80 (1H, d, J=16.2Hz), 7.61 (2H, d, J=8.6Hz), 7.51 (2H, d, J=8.6Hz), 7.39 (1H, d, J=8.8Hz), 7.24-7.33 (2H, m), 6.49 (1H, d, J=16.2Hz), 5.12 (2H, s), 4.31 (1H, m), 2.95 (2H, m), 1.77 (2H, m), 1.26 (3H, d, J=6.6Hz), 1.09 (3H, d, J=6.6Hz), 0.82 (3H, t, J=7.2Hz)

Example 20(24)

4-[2-(N-isopropyl-pentylsulfonylamino)-5-trifluoromethylphenoxymethyl]cinnamic acid

[0367]

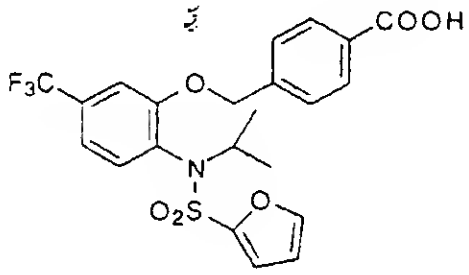


TLC : Rf 0.27 ($CHCl_3$: MeOH : AcOH= 100 : 5 : 1),
NMR : δ 7.80 (1H, d, J=16.0Hz), 7.61 (2H, d, J=8.4Hz), 7.51 (2H, d, J=8.4Hz), 7.39 (1H, m), 7.24-7.33 (2H, m), 6.48 (1H, d, J=16.0Hz), 5.12 (2H, s), 4.31 (1H, sept, J=6.6Hz), 2.96 (2H, m), 1.72 (2H, m), 1.26 (3H, d, J=6.6Hz), 1.05-1.23 (7H, m), 0.83 (3H, t, J=6.2Hz).

Example 20(25)

4-[2-(N-isopropyl-2-furanylsulfonylamino)-5-trifluoromethylphenoxymethyl]benzoic acid

[0368]

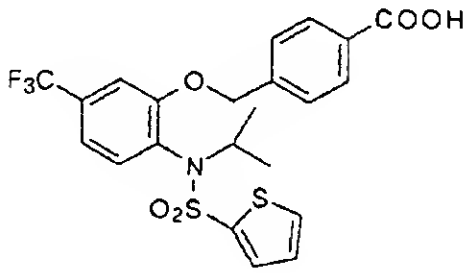


TLC : Rf 0.22 (hexane . AcOEt = 1 : 1),
NMR : δ 8.15 (2H, d,J=8Hz), 7.59 (2H, d, J=8Hz), 7.46 (1H, dd, J=2, 1Hz), 7.23 (3H, m), 6.94 (1H, dd, J=3.5, 1Hz), 6.44 (1H, dd, J=3.5, 2Hz), 5.18 (2H, s), 4.49 (1H, m), 1 10 (6H, dd, J=7, 2.5Hz).

Example 20(26)

4-[2-(N-isopropyl-2-thienylsulfonylamino)-5-trifluoromethylphenoxymethyl]benzoic acid

[0369]

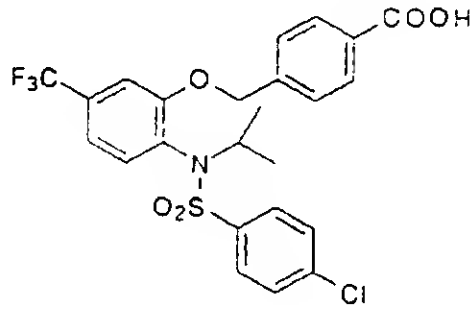


TLC : Rf 0.24 (hexane : AcOEt = 1 : 1);
NMR : δ 8.15 (2H, d, J=8.5Hz), 7.57 (2H, d, J=8.5Hz), 7.54-7.51 (2H, m), 7.25 (3H, m), 7.01-6.99 (1H, m), 5.19 (2H, s), 4.49-4.44 (1H, m), 1.10 (6H, d, J=6.5Hz).

Exemple 20(27)

4-[2-(N-isopropyl-4-chlorophenylsulfonylamino)-5-trifluoromethylphenoxymethyl]benzoic acid

[0370]

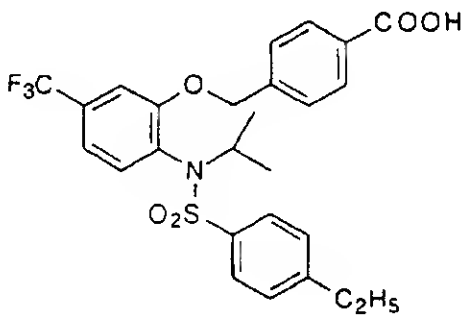


TLC : Rf 0.43 ($CHCl_3$: MeOH = 10 : 1);
NMR ($DMSO-d_6$) : δ 7.93 (2H, d, J=8.4Hz), 7.73 (2H, d, J=8.4Hz), 7.56 (1H, s), 7.50-7.28 (6H, m), 5.22 (2H, s), 4.38 (1H, sept, J=6.6Hz), 1.00 (3H, d, J=6.6Hz), 0.93 (3H, d, J=6.6Hz).

Example 20(28)

4-[2-(N-isopropyl-4-ethylphenylsulfonylamino)-5-trifluoromethylphenoxymethyl]benzoic acid

[0371]

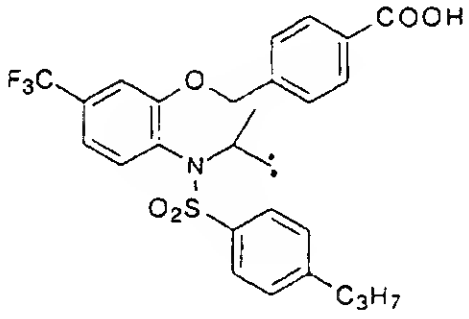


TLC : Rf 0.40 ($CHCl_3$: MeOH = 10 : 1);
NMR (DMSO-d_6) : δ 7.94 (2H, d, J=8.4Hz), 7.66 (2H, d, J=8.4Hz), 7.55 (1H, d, J=1Hz), 7.49 (2H, d, J=8.4Hz), 7.39 (1H, dd, J=8.4Hz, 1Hz), 7.32 (1H, d, J=8.4Hz), 7.23 (2H, d, J=8.4Hz), 5.25 (2H, s), 4.14 (1H, sept, J=6.6Hz), 2.61 (2H, q, J=7.4Hz), 1.14 (3H, t, J=7.4Hz), 1.00 (3H, d, J=6.6Hz), 0.93 (3H, d, J=6.6Hz).

Example 20(29)

4-[2-(N-isopropyl-4-propylphenylsulfonylamino)-5-trifluoromethylphenoxymethyl]benzoic acid

[0372]

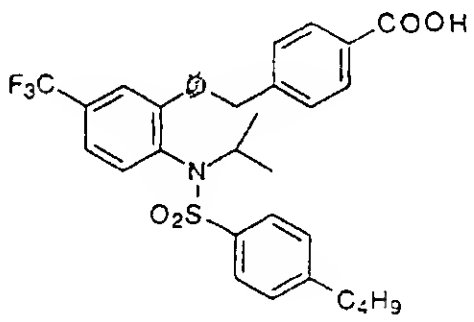


TLC : Rf 0.41 ($CHCl_3$: MeOH = 10 1);
NMR (DMSO-d_6) : δ 7.94 (2H, d, J=8.4Hz), 7.65 (2H, d, J=8.4Hz), 7.55 (1H, d, J=1Hz), 7.50 (2H, d, J=8.4Hz), 7.39 (1H, dd, J=8.4Hz, 1Hz), 7.32 (1H, d, J=8 4Hz), 7.20 (2H, d, J=8.4Hz), 5.25 (2H, s), 4.13 (1H, sept, J=6.6Hz), 2.55 (2H, t, J=7.4Hz), 1.54 (2H, tq, J=7 4Hz, 7 4Hz), 0.97 (3H, d, J=6.6Hz), 0.90 (3H, d, J=6.6Hz), 0.84 (3H, t, J=7.4Hz).

Example 20(30)

4-[2-(N-isopropyl-4-butylphenylsulfonylamino)-5-trifluoromethylphenoxymethyl]benzoic acid

[0373]



TLC : Rf 0.41 ($CHCl_3$: MeOH = 10 : 1);
NMR (DMSO-d_6) : δ 7.94 (2H, d, J=8.4Hz), 7.65 (2H, d, J=8.4Hz), 7.55 (1H, d, J=1Hz), 7.49 (2H, d, J=8.4Hz), 7.38 (1 H, dd, J=8.4Hz, 1Hz), 7.33 (1H, d, J=8.4Hz), 7.20 (2H, d, J=8.4Hz), 5.24 (2H, s), 4.14 (1H, sept, J=6.6Hz), 2.57 (2H, t, J=7.4Hz), 1.49 (2H, m), 1.25 (2H, m), 0.98 (3H, d, J=6.6Hz), 0.89 (3H, d, J=6.6Hz), 0.87 (3H, t, J=7.4Hz).

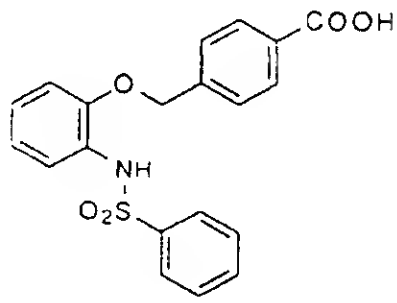
Example 21-21(16)

[0374] By using 2-nitrophenol or the corresponding compounds, the title compounds having the following physical data were obtained by the same procedure as Reference Example 6→Reference Example 12→Reference Example 2→Example 2.

Example 21

4-(2-phenylsulfonylaminophenoxymethyl)benzoic acid

[0375]

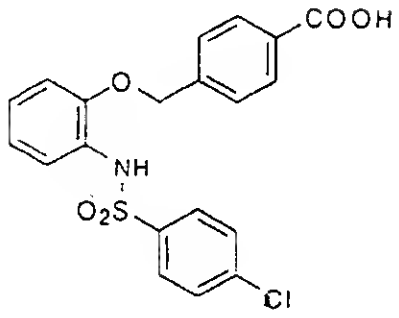


TLC : Rf 0.35 (AcOEt : hexane : AcOH = 6 : 13 : 1);
NMR (DMSO-d_6) : δ 12.86 (1H, brs), 9.53 (1H, brs), 7.91 (2H, d, J=8.0Hz), 7.66 (2H, d, J=8.0Hz), 7.52 (1H, t, J=7.0Hz), 7.45-7.25 (5H, m), 7.08 (1H, t, J=9.0Hz), 6.95-6.80 (2H, m), 4.91 (2H, s).

Example 21(1)

4-[2-(4-chlorophenylsulfonylamino)phenoxymethyl]benzoic acid

[0376]

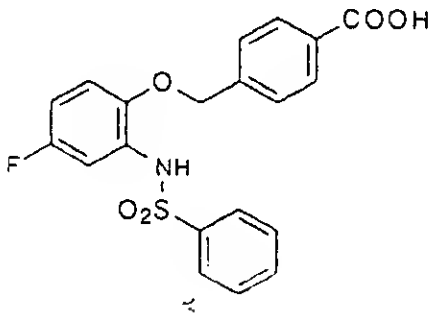


TLC : Rf 0.39 (AcOEt : hexane : AcOH= 6 : 13 : 1);
NMR (DMSO-d_6) : δ 12.85 (1H, brs), 9.68 (1H, brs), 7.93 (2H, d, J=8.5Hz), 7.60 (2H, d, J=8.5Hz), 7.36 (4H, d, J=8.5Hz), 7.35-7.25 (1H, m), 7.12 (1H, dt, J=7.5, 2.0Hz), 6.96-6.85 (2H, m), 4.92 (2H, s).

Example 21(2)

4-(2-phenylsulfonylamino-4-fluorophenoxymethyl)benzoic acid

[0377]

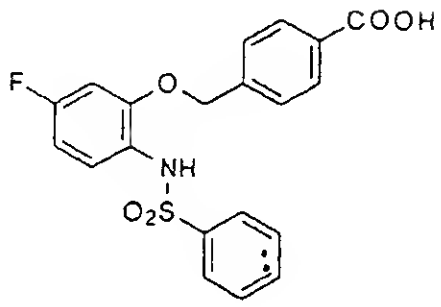


TLC : Rf 0.37 (AcOEt : hexane : AcOH= 6 : 13 : 1);
NMR (DMSO-d_6) : δ 12.95 (1H, brs), 9.90 (1H, brs), 7.90 (2H, d, J=8.5Hz), 7.72 (2H, d, J=7.0Hz), 7.58 (1H, m), 7.46 (2H, t, J=7.5Hz), 7.37 (2H, d, J=8.5Hz), 7.10 (1H, d, J=9.5Hz), 6.92 (2H, d, J=7.0Hz), 4.95 (2H, s).

Example 21(3)

4-(2-phenylsulfonylamino-5-fluorophenoxymethyl)benzoic acid

[0378]

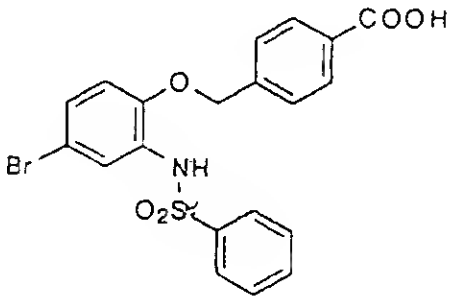


TLC : Rf 0.42 (AcOEt : hexane : AcOH= 6 : 13 : 1);
NMR (DMSO-d_6) : δ 12.95 (1H, brs), 9.65 (1H, brs), 7.91 (2H, d, J=8.5Hz), 7.60 (2H, d, J=7.0Hz), 7.52 (1H, t, J=7.0Hz), 7.39 (2H, d, J=7.5Hz), 7.35 (2H, d, J=7.5Hz), 7.26 (1H, dd, J=7.0,6.5Hz), 6.84 (1H, dd, J=11.0, 2.5Hz), 6.75 (1H, dt, J=8.5, 2.5Hz), 4.90 (2H, s).

Example 21(4)

4-(2-phenylsulfonylamino-4-bromophenoxymethyl)benzoic acid

[0379]

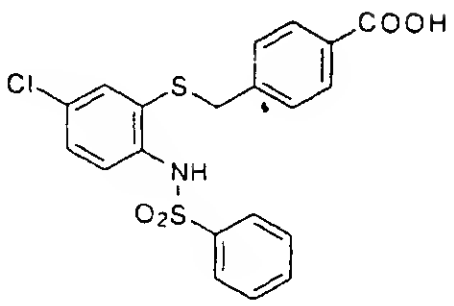


TLC . Rf 0.25 (AcOEt : hexane : AcOH= 6 : 13 : 1);
NMR (DMSO-d_6) : δ 12.97 (1H, brs), 9.97 (1H, brs), 7.90 (2H, d, J=8.0Hz), 7.69 (2H, dd, J=7.5, 2Hz), 7.58 (1H, tt, J=7.5, 2Hz), 7.46 (2H, d, J=7.5Hz), 7.39 (1H, d, J=2.5Hz), 7.36 (2H, d, J=8.0Hz), 7.27 (1H, dd, J=9.0, 2.5Hz), 6.89 (1H, d, J=9Hz), 4.97 (2H, s).

Example 21(5)

4-(2-phenylsulfonylamino-5-chlorophenylthiomethyl)benzoic acid

[0380]

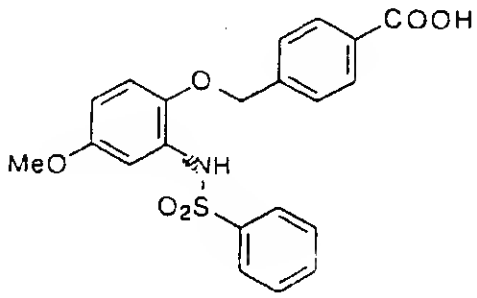


TLC : Rf 0.50 ($CHCl_3$: MeOH : AcOH= 100 : 5 : 1);
NMR : δ 7.99 (2H, d, J=8.4Hz), 7.78 (2H, m), 7.41-7.62 (5H, m), 7.23 (1H, dd, J=2.6, 8.8Hz), 7.08 (1H, d, J=2.6Hz), 7.05 (2H, d, J=8.6Hz), 3.71 (2H, s).

Example 21(6)

4-(2-phenylsulfonylamino-4-methoxyphenoxymethyl)benzoic acid

[0381]

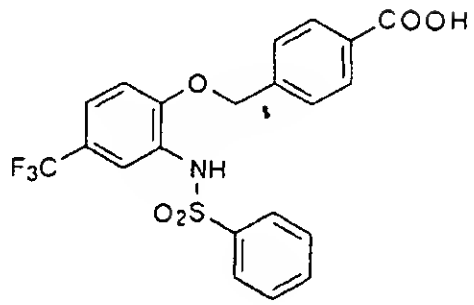


TLC : Rf 0.38 ($CHCl_3$: MeOH = 17 : 3);
NMR (DMSO-d_6) : δ 7.90 (2H, d, J=8.5Hz), 7.71 (2H, d, J=8.0Hz), 7.64-7.35 (5H, m), 6.90-6.80 (2H, m), 6.44 (1H, dd, J=9.0 and 3.0Hz), 4.89 (2 H, s), 3.65 (3 H, m).

Example 21(7)

4-(2-phenylsulfonylamino-4-trifluoromethylphenoxymethyl)benzoic acid

[0382]

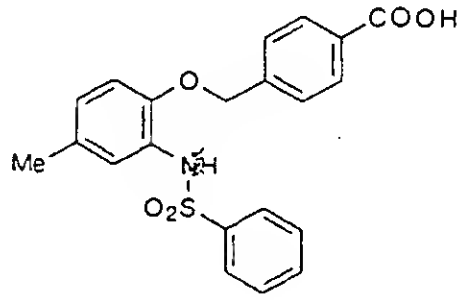


TLC : Rf 0.32 ($CHCl_3$: MeOH = 17 : 3);
NMR (DMSO-d_6) : δ 7.92 (2H, d, J=8.5Hz), 7.69 (2H, d, J=8.0Hz), 7.63-7.34 (7H, m),7.11 (1H, d, J=8.5Hz), 5.09 (2H, s).

Example 21(8)

4-(2-phenylsulfonylamino-4-methylphenoxymethyl)benzoic acid

[0383]

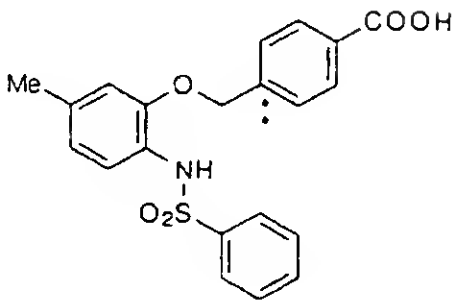


TLC : Rf 0.43 (AcOEt : hexane : AcOH= 7 : 12 : 1);
NMR (DMSO-d_6) : δ 7.89 (2H, d, J=8.0Hz), 7.66 (2H, d, J=7.0Hz), 7.60-7.48 (1H, m), 7.41 (2H, d, J=8.0Hz), 7.35 (2H, d, J=8Hz), 7.11 (1H, d, J=2.0Hz), 6.90 (1H, dd, J=8.0, 2.0Hz), 6.76 (1H, d, J=8Hz), 4.88 (2H, s), 2.19 (3H, s).

Example 21(9)

4-(2-phenylsulfonylamino-5-methylphenoxymethyl)benzoic acid

[0384]

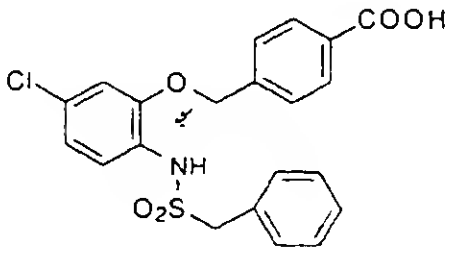


TLC : Rf 0.43 (AcOEt : hexane : AcOH= 7 : 12 : 1);
NMR (DMSO-d_6) : δ 7.91 (2H, d, J=8.5Hz), 7.62 (2H, d, J=7.0Hz), 7.57-7.45 (1H, m), 7.44-7.30 (4H, m), 7.14 (1H, d, J=8.0Hz), 6.75 (1H, s), 6.71 (1H, d, J=8.0Hz), 4.88 (2H, s), 2.21 (3H, s).

Example 21(10)

4-(2-benzylsulfonylamino-5-chlorophenoxymethyl)benzoic acid

[0385]

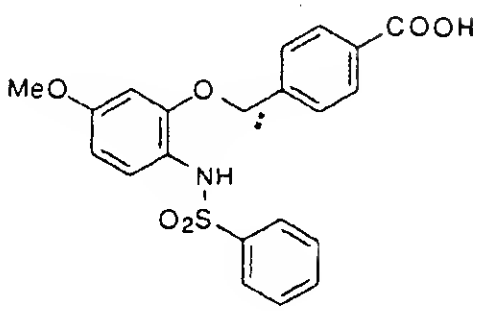


TLC : Rf 0.52 ($CHCl_3$: MeOH : AcOH= 100 : 5 : 1).
NMR (DMSO-d_6) : δ 7.96 (2H, d, J=8.0Hz), 7.67 (2H, d, J=8.0Hz), 7.29 (5H, s), 7.21 (1H, d, J=8.2Hz), 7.20 (1H, d, J=2.4Hz), 6.95 (1H, dd, J=2.4, 8.2Hz), 5.31 (2H, s), 4.38 (2H, s).

Example 21(11)

4-(2-phenylsulfonylamino-5-methoxyphenoxymethyl)benzoic acid

[0386]

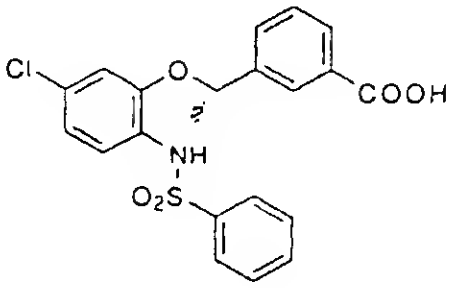


TLC : Rf 0.40 ($CHCl_3$: MeOH = 4 : 1);
NMR (DMSO-d_6) : δ 7.90 (2H, d, J=8.5Hz), 7.59 (2H, d, J=8Hz), 7.51 (1H, t, J=8Hz), 7.44-7.28 (4H, m), 7.15 (1H, d, J=8.5Hz), 6.54-6.47 (2H, m), 4.86 (2H, s), 3.69 (3H, s).

Example 21(12)

3-(2-phenylsulfonylamino-5-chlorophenoxymethyl)benzoic acid

[0387]

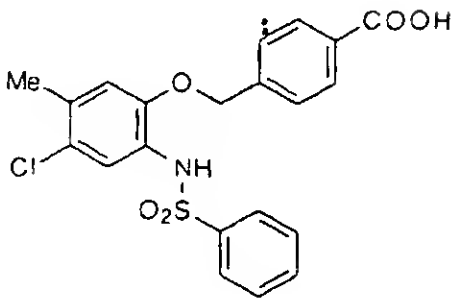


TLC : Rf 0.48 (AcOEt : hexane : AcOH= 7 : 12 : 1);
NMR (DMSO-d_6) : δ 13.03 (1H, brs), 9.80 (1H, brs), 7.98 (1H, s), 7.95-7.86 (1H, m), 7.66 (2H, d, J=7.0Hz), 7.58-7.46 (3H, m), 7.40 (2H, t, J=7.0Hz), 7.27 (1H, d, J=8.5Hz), 7.07 (1H, d, J=2.5Hz), 6.96 (1H, dd, J=8.5, 2.5Hz), 4.96 (2H, s)

Example 21(13)

4-(2-phenylsulfonylamino-4-chloro-5-methylphenoxymethyl)benzoic acid

[0388]

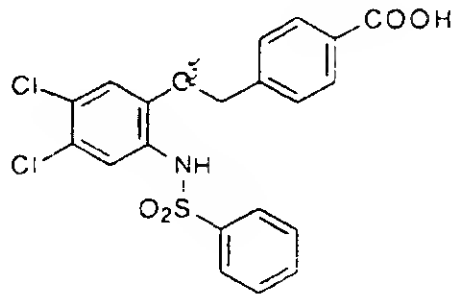


TLC : Rf 0.44 ($CHCl_3$: MeOH = 4 : 1);
NMR ($DMSO-d_6$) : δ 7.91 (2H, d, J=8Hz), 7.66 (2H, d, J=7Hz), 7.55 (1H, t, J=7.5Hz), 7.47-7.30 (4H, m), 7.25 (1H, s), 6.98 (1H, s), 4.93 (2H, s), 2.23 (3H, s).

Example 21(14)

4-(2-phenylsulfonylamino-4,5-dichlorophenoxymethyl)benzoic acid

[0389]

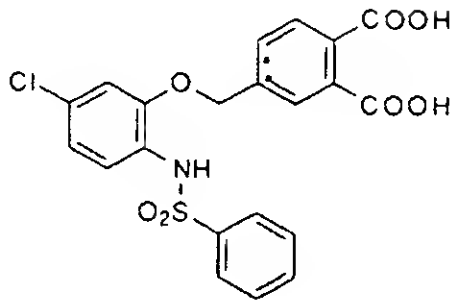


TLC : Rf 0.42 ($CHCl_3$: MeOH = 4 · 1);
NMR ($DMSO-d_6$) : δ 7.92 (2H, d, J=8Hz), 7.69 (2H, d, J=7.5Hz), 7.58 (1H, t, J=7.5Hz), 7.50-7.31 (5 H, m), 7.26 (1H, s), 5.01 (2H, s).

Example 21(15)

4-(2-phenylsulfonylamino-5-chlorophenoxymethyl)phthalic acid

[0390]

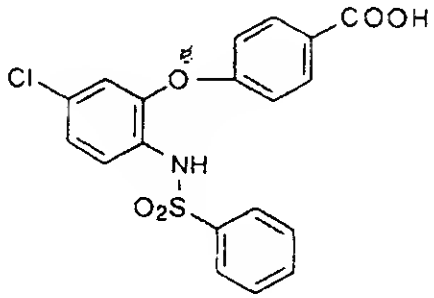


TLC : Rf 0.36 ($CHCl_3$: MeOH : AcOH= 15 : 4 : 1);
NMR ($DMSO-d_6$) : δ 13.23 (2H, brs), 9.86 (1H, s), 7.74-7.58 (4H, m), 7.56-7.30 (4H, m), 7.29 (1H, d, J=8.5Hz), 7.06 (1H, d, J=2.0Hz), 6.98 (1H, dd, J=8.5, 2Hz), 4.94 (2H, s).

Example 21(16)

4-(2-phenylsulfonylamino-5-chlorophenoxy)benzoic acid

[0391]



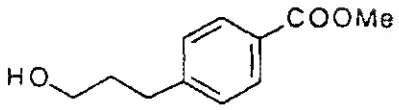
TLC : Rf 0.46 ($CHCl_3$: MeOH = 9 : 1),
NMR : δ 7.99 (2H, d, J=9.0Hz), 7.8-7.7 (3H, m), 7.6-7.5 (1H, m), 7.5-7.3 (2H, m), 7.15 (1H, dd, J=2.2, 8.8Hz), 6.97 (1H, s), 6.77 (1H, d, J=2.2Hz), 6.65 (2H, d, J=9.0Hz).

Reference Example 18

Methyl 4-[3-(2-nitro-5-chlorophenoxy)propyl]benzoate

(a) OH having compound

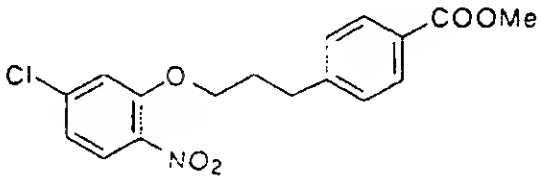
[0392]



[0393] To a solution of methyl 4-(2-methoxycarbonylethyl)benzoate (1.0 mg) in mixture of THF-MeOH (12 ml; THF : MeOH = 5 : 1), sodium boron hydride (85 mg) was added. The mixture was stirred for 19 hours at room temperature. To the reaction mixture, emmonium chloride wes edded. After en excess of reagent was decomposed, the mixture was extracted with ethyl acetate. The organic layer was washed, dried over and concentrated under the reduced pressure. The residue was purified on silica gel column chromatography (AcOEt : hexane = 2 : 3) to give the OH having compound (692 mg) having the following physical data. TLC : Rf 0.38 (hexane : AcOEt = 1 : 1).

(b) title compound

[0394]



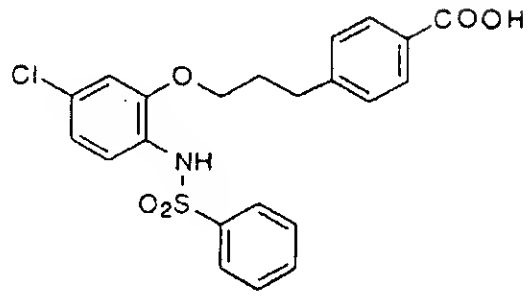
[0395] To a solution of 2-nitro-5-chlorophenol (150 mg) in THF (2.0 ml), the OH having compound prepared in the above (a) (168 mg) and triphenylphosphine (227 mg) were added in a stream of argon. After then, DEAD (136 ml) was added dropwise thereto et 0°C. The reaction mixture wes stirred for 24 hours et room temperature. After stirring, the mixture was quenched by adding iced water and extracted with ethyl acetate. After stirring, the mixture was quenched by adding iced water and extracted with ethyl acetate. The organic layer was washed, dried over and concentrated under the reduced pressure. The residue was purified on silica gel column chrometography (hexane : AcOEt = 10 : 1 5 : 1) to give the title compound (309 mg) having the following physical data.

TLC : Rf 0.24 (hexane : AcOEt = 5 : 1).

Example 22

4-[3-(2-phenylsulfonylamino-5-chlorophenoxy)propyl]benzoic acid

[0396]



[0397] By using methyl 4-[3-(2-nitro-5-chlorophenoxy)propyl]benzoate (prepared in Reference Example 18.), the title compound having the following physical data was obtained by the same procedure as Reference Example 12→Reference Example 2→Example 2.

TLC : Rf 0.41 ($CHCl_3$: MeOH : AcOH= 100 : 5 : 1);
NMR : δ 8.04 (2H, d, J=8.4Hz), 7.73 (2H, m), 7.50 (2H, m), 7.40 (2H, m), 7.21 (2H, d, J=8.2Hz), 5.92 (1H, brs), 6.91 (1H, dd, J=2.2, 8.6Hz), 6.67 (1H, d, J=2.2Hz), 3.75 (2H, t, J=6.2Hz), 2.70 (2H, t, J=7.0Hz), 1.98 (2H, m).

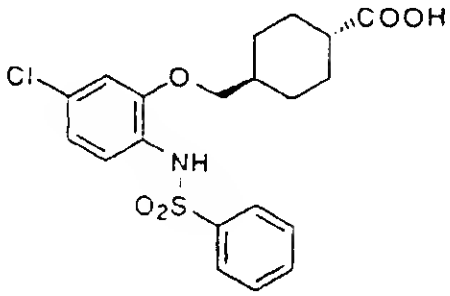
Example 22(1)-22(4)

[0398] By using corresponding diester, halfester or 4-acetylbenzoic acid, the title compounds having the following physical data were obtained by the same procedure as Reference Example 18→Reference Example 12→Reference Example 2→Example 2.

Example 22(1)

trans-4-(2-phenylsulfonylamino-5-chlorophenoxymethyl)cyclohexanoic acid

[0399]



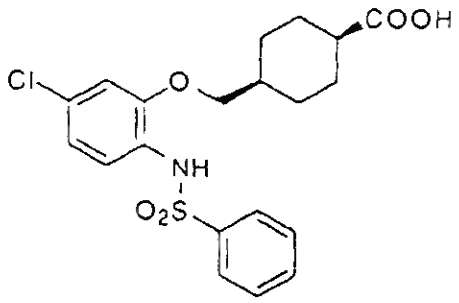
TLC : Rf 0.39 ($CHCl_3$: MeOH : AcOH= 100 : 5 : 1);
NMR : δ 7.70 (2H, m), 7.36-7.59 (4H, m), 6.92 (1H, brs), 6.91 (1H, dd, J=2.2, 8.4Hz), 6.70 (1H, d, J=2.2Hz), 3.55

(2H, d, J=6.2Hz), 2.31 (1H, tt, J=3.8, 12.0Hz), 2.00-2.19 (2H, m), 1.35-1.85 (5H, m), 0.95 (2H, m).

Example 22(2)

cis-4-(2-phenylsulfonylamino-5-chlorophenoxymethyl)cyclohexanoic acid

[0400]

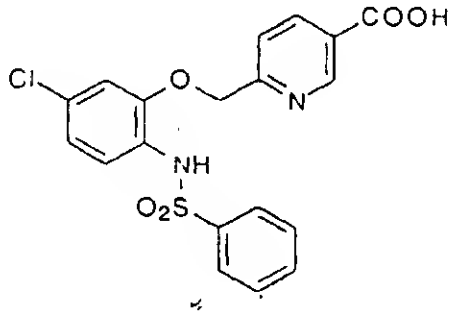


TLC : Rf 0.53 ($CHCl_3$: MeOH : AcOH= 100 : 5 : 1);
NMR : δ 7.70 (2H, m), 7.35-7.57 (4H, m), 6.89 (1H, dd, J=2.2, 8.6Hz), 6.84 (1H, brs), 6.69 (1H, d, J=2.2Hz), 3.58 (2H, d, J=6.4Hz), 2.70 (1H, m), 1.98-2.15 (2H, m), 1.43-1.80 (5H, m), 1.15-1.40 (2H, m).

Example 22(3)

6-(2-phenylsulfonylamino-5-chlorophenoxymethyl)nicotinic acid

[0401]

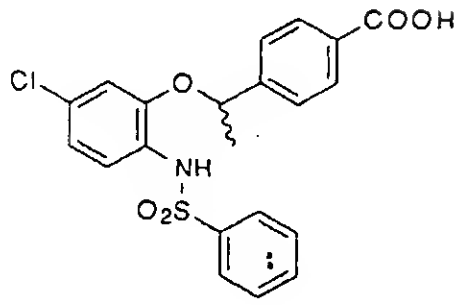


TLC : Rf 0.40 ($CHCl_3$: MeOH : AcOH= 100 : 10 : 1),
NMR (DMSO-d_6) : δ 9.90 (1H, brs), 9.02 (1H, d, J=1.6Hz), 8.27 (1H, dd, J=2.2, 8.4Hz), 7.62 (2H, m), 7.49 (2H, m), 7.31-7.39 (2H, m), 7.31 (1H, d, J=8.6Hz), 7.08 (1H, d, J=2.2Hz), 7.02 (1H, dd, J=2.2, 8.6Hz), 4.96 (2H, s).

Example 22(4)

4-[1RS-(2-phenylsulfonylamino-5-chlorophenoxy)ethyl]benzoic acid

[0402]

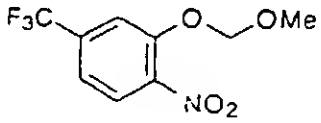


TLC : Rf 0.48 ($CHCl_3$: MeOH = 9 : 1);
NMR : δ 12.0-10.0 (1H, br), 8.00 (2H, d, J=8.4Hz), 7.78 (2H, d, J=7.8Hz), 7.7-7.4 (4H, m), 7.1-7.0 (3H, m), 6.88 (1H, dd, J=2.2, 8.8Hz), 6.45 (1H, s), 5.14 (1H, q, J=6.4Hz), 1.50 (3H, d, J =6.4Hz).

Reference Example 19

2-nitro-5-trifluoromethylphenyl methoxymethyl ether

[0403]



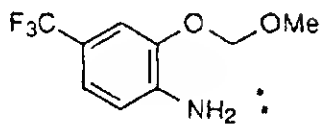
[0404] To a solution of 2-nitro-5-trifluoromethylphenol (400 mg) in DMF (4.0 ml), sodium hydride (77 mg) was added at 0°C in a stream of argon. The mixture was stirred for 30 minutes After stirring, methoxymethyl chloride (147 ml) was added dropwise thereto. The mixture was stirred for 20 minutes. The reaction mixture was quenched by iced water and extracted with ethyl acetate. The layer containing ethyl acetate was washed, dried over and concentrated under the reduced pressure. The residue was purified on silica gel column chromatography (hexane : AcOEt = 20 : 1) to give the title compound (353 mg) having the following physical data.

TLC Rf 0.44 (hexane : AcOEt = 10 : 1).

Reference Example 20

2-amino-5-trifluoromethylphenyl methoxymethyl ether

[0405]



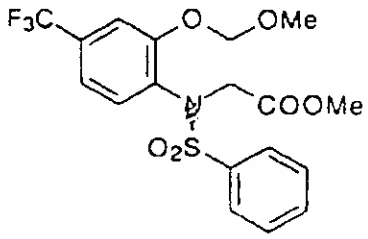
[0406] To a solution of 2-nitro-5-trifluoromethylphenyl methoxymethyl ether (353 mg; prepared in Reference Example 19.) in MeOH (3.5 ml), 10%Pd-C (30 mg) was added in a stream of argon. The mixture was stirred vigorously at room tempereture under hydrogen atmosphere. The reaction mixture was filtered through celite and concentrated under the reduced pressure to give the title compound (313 mg) having the following physical data.

TLC : Rf 0.44 (hexane : AcOEt = 3 : 1).

Reference Example 21

Methyl N-(2-methoxymethoxy-4-trifluoromethylphenyl)-phenylsulfonyleminoacetete

[0407]



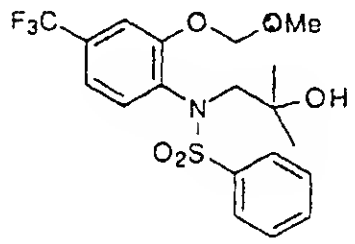
[0408] By using 2-amino-5-trifluoromethylphenyl methoxymethyl ether (313 mg; prepared in Reference Example 20.), the title compound (625 mg) heving the following physical data was obteined by the same procedure as Reference Example 2→Example 17.

TLC : Rf 0.66 (benzene : acetone = 9 . 1).

Reference Example 22

1,1-dimethyl-2-[N-(2-methoxymethoxy-4-trifluoromethylphenyl)-phenylsulfonylamino]ethanol

[0409]

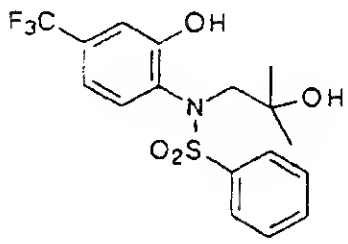


[0410] To a solution of methyl N-(2-methoxymethoxy-4-trifluoromethylphenyl)-phenylsulfonylaminoacetate (525 mg; prepared in Reference Example 21.) in THF (6.0 ml), methylmagnesium bromide (2.67 ml) was added dropwise in a stream of argon at 0°C. The mixture was stirred for 30 minutes. The reaction mixture was quenched by iced water, extrected with ethyl acetate, washed, dried over and concentrated under the reduced pressure. The residue wes purified on silica gel column chromatography (hexane : AcOEt = 2 : 1) to give the title compound (380 mg) having the following physical data. TLC : Rf 0.26 (hexane : AcOEt = 2 : 1).

Reference Example 23

1,1-dimethyl-2-[N-(2-hydroxy-4-trifluoromethylphenyl)-phenylsulfonylamino]ethanol

[0411]



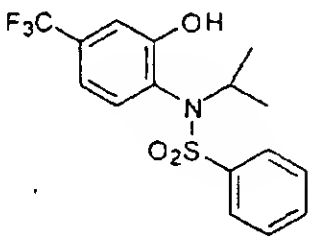
[0412] To a solution of 1,1-dimethyl-2-[N-(2-methoxymethoxy-4-trifluoromethylphenyl)-phenylsulfonylamino]ethanol (380 mg; prepared in Reference Example 22.) in THF (4.0 ml), 6N HCl (0.8 ml) was added. The mixture was stirred for 2 days at room temperature. The reection mixture wes diluted with ethyl ecetate, washed, dried over end concentrated under the reduced pressure. The residue was purified on silica gel column chromatography (hexane : AcOEt = 2 : 1) to give the title compound (291 mg) having the following physical data.

TLC : Rf 0.29 (benzene : ecetone = 9 : 1).

Reference Example 24

2-(N-isopropyl-phenylsulfonylamino)-5-trifluoromethylphenol

[0413]



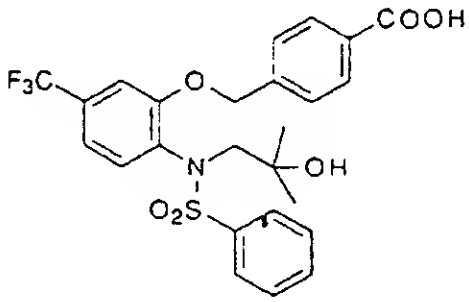
[0414] By using 2-amino-5-trifluoromethylphenyl methoxymethyl ether (prepared in Reference Example 20.), the title compound having the following physical data was obtained by the same procedure as Reference Example 2→Example 17→Reference Example 23.

TLC : Rf 0.57 (hexane : AcOEt = 5 : 2).

Example 23

4-[2-[N-(2-hydroxy-2-methylpropyl)-phenylsulfonylamino]-5-trifluoromethylphenoxymethyl]benzoic acid

[0415]



[0416] By using 1,1-dimethyl-2-[N-(2-hydroxy-4-trifluoromethylphenyl)-phenylsulfonylamino]ethanol (prepared in Reference Example 23), the title compound having the following physical data wes obtained by the seme procedure as Reference Example 6→Example 2.

TLC : Rf 0.48 ($CHCl_3$: MeOH : AcOH= 100 : 5 : 1).
NMR (CD_3COCD_3) : δ 8.03 (2H, brd, J=8.2Hz), 7 47-7 66 (4H, m), 7.30-7.47 (6H, m), 5.21 (1H, m), 4.89 (1H, m), 3.79 (2H, s), 1.20 (6H, s).

Exemple 23(1)-23(3)

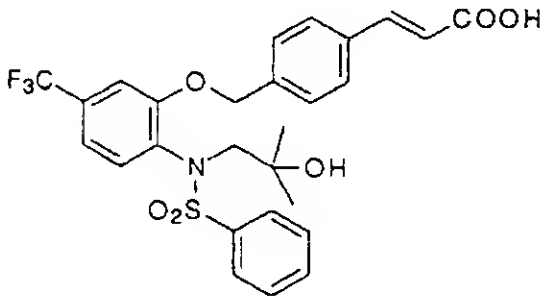
[0417] By using 2-[N-(2-hydroxy-2-methylpropyl)-phenylsulfonylamino]-5-trifluoromethylphenol (prepared in Reference Example 23.), the title compounds having the following physical data were obtained by the same procedure as

Reference Example 6→Example 2.

Example 23(1)

4-[2-[N-(2-hydroxy-2-methylpropyl)-phenylsulfonylamino]-5-trifluoromethylphenoxymethyl]cinnamic acid

[0418]

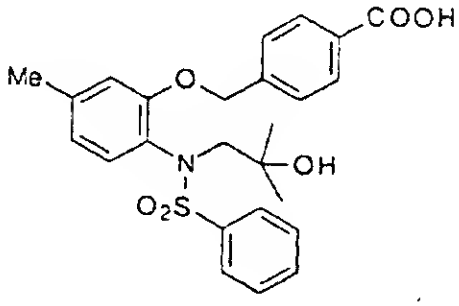


TLC : Rf 0.53 ($CHCl_3$: MeOH = 9 : 1);
NMR : δ 7.80 (1H, d, J=16.0Hz), 7.54 (6H, m), 7.35 (6H, m), 6.49 (1H, d, J=16.0Hz), 4.99 (1H, m), 4.81 (1H, m), 3.63 (2H, m), 1.21 (6H, s).

Example 23(2)

4-[2-[N-(2-hydroxy-2-methylpropyl)-phenylsulfonylamino]-5-methylphenoxymethyl]benzoic acid

[0419]

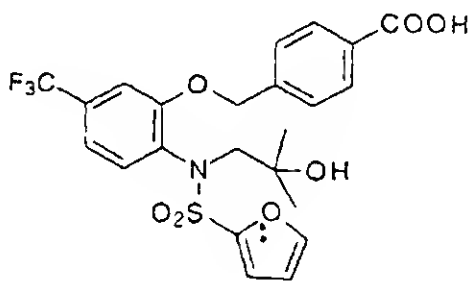


TLC : Rf 0.45 ($CHCl_3$: MeOH = 9 : 1);
NMR : δ 8.09 (2H, d, J=8.4Hz), 7.60 (2H, m), 7.28-7.44 (5H, m), 7.06 (1H, m), 6.71 (2H, m), 5.00 (1H, d, J=12.8Hz), 4.74 (1H, d, J=12.8Hz), 3.69 (1H, d, J=14.2Hz), 3.57 (1H, d, J=14.2Hz), 2.33 (3H, s), 2.13 (1H, s), 1.25 (3H, bs), 1.19 (3H, bs)

Example 23(3)

4-[2-[N-(2-hydroxy-2-methylpropyl)-2-furanylsulfonylamino]-5-trifluoromethylphenoxymethyl]benzoic acid

[0420]

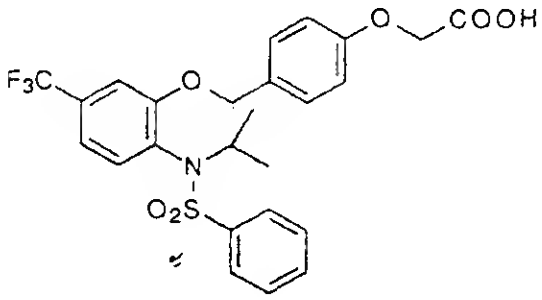


TLC : Rf 0.42 ($CHCl_3$: MeOH = 9 : 1);
NMR : δ 8.15 (2H, d, J=8.4Hz), 7.52 (2H, d, J=8.4Hz), 7.21-7.34 (4H, m), 6.82 (1H, m), 6.38 (1H, m), 5.12 (2H, m), 3.76 (2H, m), 2.12 (1H, s), 1.23 (6H, bs).

Example 24

4-[2-(N-isopropyl-phenylsulfonylamino)-5-trifluoromethylphenoxymethyl]phenoxy acetic acid

[0421]



[0422] By using 2-(N-isopropyl-phenylsulfonylamino)-5-trifluoromethylphenol (prepared in Reference Example 24.), the title compound heving the following physicel data wes obteined by the same procedure es Reference Exemple 18 (b)→Example 2.

TLC : Rf 0.39 (AcOEt : hexene : AcOH= 9 : 10 : 1);
NMR : δ 7.80 (2H, d, J=7.5Hz), 7.49 (1H, t, J=7.5Hz), 7.40-7.20 (7H, m), 6.95 (2H, d, J=8.5Hz), 4.98 (2H, s), 4.72 (2H, s), 4.28 (1H, qn, J=6.5Hz), 1.06 (3H, d, J=6.5Hz), 1.01 (3H, d, J=6.5Hz).

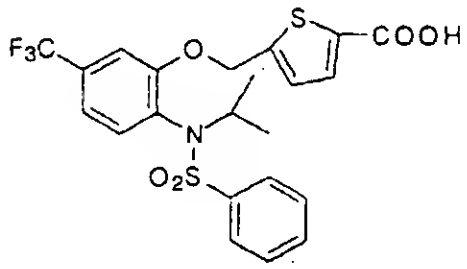
Exemple 24(1)-24(10)

[0423] By using the corresponding compounds, the title compounds having the following physical data were obtained by the same procedure as Reference Example 18 (b)→Example 2.

Example 24(1)

5-[2-(N-isopropyl-ph nylsulfonylamino)-5-trifluoromethylphenoxymethyl]thiophene-2-carboxylic acid

[0424]

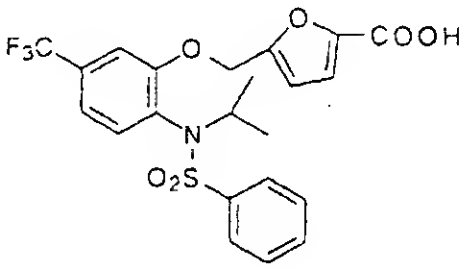


TLC : Rf 0.54 ($CHCl_3$: MeOH : AcOH= 90 : 9 : 1);
NMR : δ 7.9-7.7 (3H, m), 7.6-7.3 (3H, m), 7.3-7.2 (3H, m), 7.16 (1H, d, J=4.0Hz), 5.20 (2H, s), 4.5-4.3 (1H, m), 1.10 (3H, d, J=3.8Hz), 1.32 (3H, d, J=3.8Hz).

Example 24(2)

5-[2-(N-isopropyl-phenylsulfonylamino)-5-trifluoromethylphenoxymethyl]furan-2-carboxylic acid

[0425]

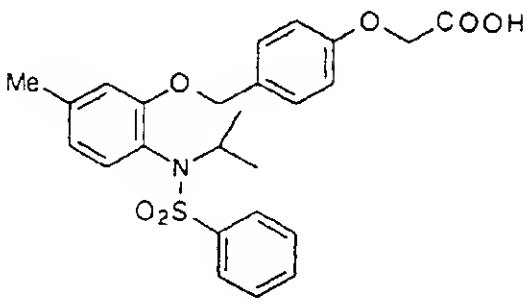


TLC : Rf 0.17 ($CHCl_3$: MeOH = 5 : 1);
NMR : δ 7.76 (2H, d, J=8Hz), 7.54-7.29 (3H, m), 7.29-7.13 (4H, m), 6.52 (1H, m), 5.00 (2H, s), 4.31 (1H, m), 0.98 (6H, m).

Example 24(3)

4-[2-(N-isopropyl-phenylsulfonylamino)-5-methylphenoxymethyl]phenoxyacetic acid

[0426]

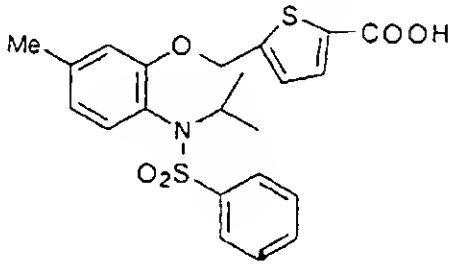


TLC : Rf 0.09 (AcOEt);
NMR : δ 7.81 (2H, d, J=7.5 Hz), 7.50-7.30 (5H, m), 7.00-6.91 (3H, m), 6.82-6.73 (2H ,m), 4.91 (2H, s), 4.71 (2H, s), 4.27 (1H, sept, J=7Hz), 2.36 (3H, s), 1.05 (3H, d, J=7Hz), 1.01 (3H, d, J=7Hz).

Example 24(4)

5-[2-(N-isopropyl-phenylsulfonylamino)-5-methylphenoxymethyl]thiophene-2-carboxylic acid

[0427]

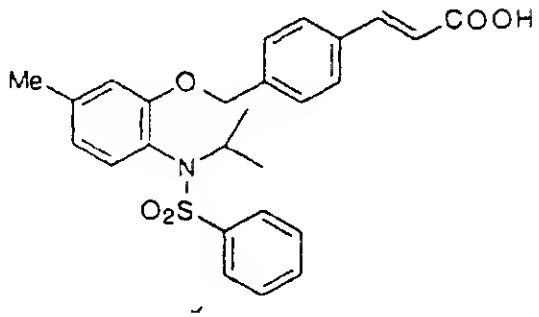


TLC : Rf 0.30 ($CHCl_3$: MeOH = 9 . 1).
NMR . δ 7.9-7.7 (3H, m), 7.5-7.4 (1H, m), 7.4-7.3 (2H, m), 7.12 (1H, d, J=3.6Hz), 7.01 (1H, d, J=8.2Hz), 6.9-6.7 (2H, m), 5.12 (2H, s), 4.5-4.3 (1H, m), 2.38 (3H, s), 1.51 (3H, d, J=2.4Hz), 1.05 (3H, d, J=2.4Hz).

Example 24(5)

4-[2-(N-isopropyl-phenylsulfonylamino)-5-methylphenoxymethyl]cinnamic acid

[0428]

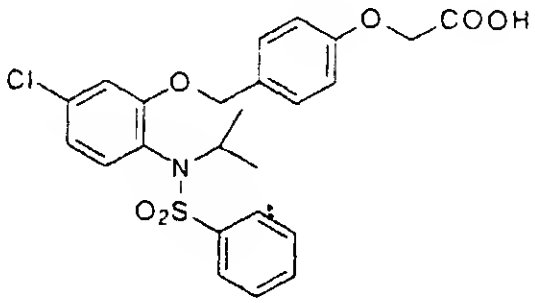


TLC : Rf 0.39 (hexane : AcOEt = 1 : 2);
NMR : δ 7.86-7.78 (3H, m), 7.60-7.26 (7H, m), 6.97 (1H, d, J=8Hz), 6.80-6.74 (2H, m), 6.48 (1H, d, J=16Hz), 5.01 (2H, s), 4.36 (1H, sept., J=6.5Hz), 1.05 (6H, d, J=6.5Hz).

Example 24(6)

4-[2-(N-isopropyl-phenylsulfonylamino)-5-chlorophenoxymethyl]phenoxyacetic acid

[0429]

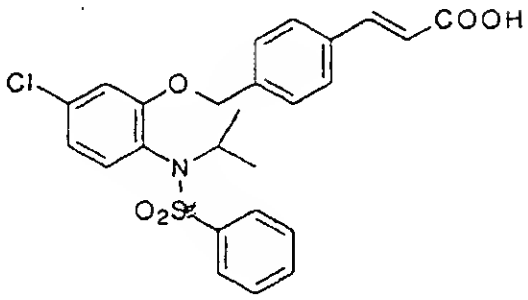


TLC : Rf 0.10 ($CHCl_3$: MeOH = 10 : 1),
NMR : δ 7.80-7.76 (2H, m), 7.52-7.44 (1H, m), 7.35-7.26 (4H, m), 7.05-6.91 (5H, m), 4.91 (2H, s), 4.72 (2H, s), 4.28 (1H, sept., J=7Hz), 1.05 (3H, d, J=7Hz), 1.00 (2H, d, J=7Hz).

Example 24(7)

4-[2-(N-isopropyl-phenylsulfonylamino)-5-chlorophenoxymethyl]cinnamic acid

[0430]

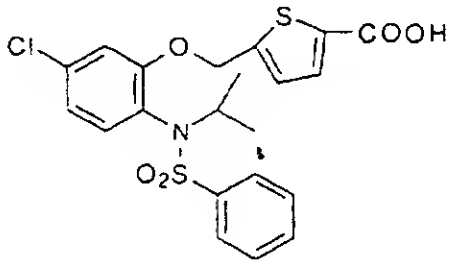


TLC : Rf 0.31 (hexane : AcOEt = 1 : 1);
NMR : δ 7.85-7.77 (2H, m), 7.60-7.35 (7H, m), 7.05-6.90 (3H, m), 6.48 (1H, d, J=16Hz), 5.01 (2H, s), 4.36 (1H, sept., J=6.5Hz), 1.04 (6H, d, J=7Hz).

Example 24(8)

5-[2-(N-isopropyl-phenylsulfonylamino)-5-chlorophenoxymethyl]thiophene-2-carboxylic acid

[0431]

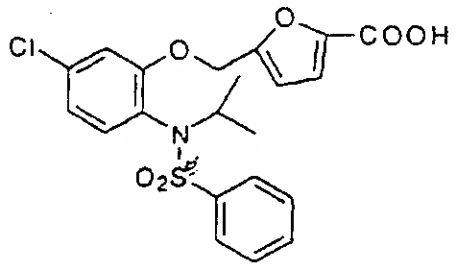


TLC : Rf 0.42 ($CHCl_3$: MeOH = 9 . 1);
NMR : δ 7.8-7.7 (3H, m), 7.5-7.3 (3H, m), 7.2-6.9 (4H, m), 5.15 (1H, d, J=13.2Hz), 5.08 (1H, d, J=13.2Hz), 4.5-4.3 (1H, m), 5.5-4.0 (1H, br), 1.08 (3H, d, J=2.6Hz), 1.05 (3H, d, J=2.6Hz).

Example 24(9)

5-[2-(N-isopropyl-phenylsulfonylamino)-5-chlorophenoxymethyl]furan-2-carboxylic acid

[0432]

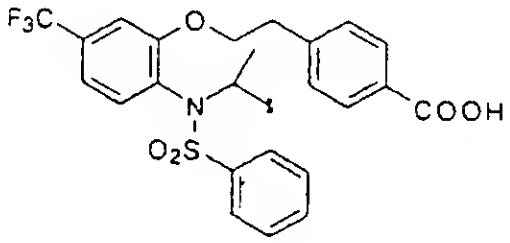


TLC : Rf 0.37 ($CHCl_3$: MeOH = 9 : 1);
NMR : δ 7.9-7.7 (2H, m), 7.6-7.4 (3H, m), 7.31 (1H, d, J=3.4Hz), 7.0-6.9 (3H, m), 6.63 (1H, d, J=3.4Hz), 5.03 (1H, d, J=13.2Hz), 4.96 (1H, d, J=13.2Hz), 5.5-4.5 (1H, br), 4.4-4.2 (1H, m), 1.03 (6H, d, J=6.6Hz).

Example 24(10)

4-[2-[2-(N-isopropyl-phenylsulfonylamino)-5-trifluoromethylphenoxy]ethyl]benzoic acid

[0433]

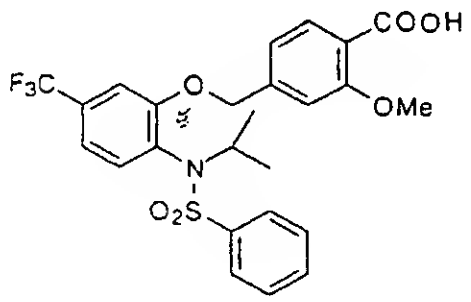


TLC : Rf 0.40 ($CHCl_3$: MeOH = 9 : 1);
NMR : δ 8.07 (2H, d, J=8.5Hz), 7.83 (2H, d, J=7Hz), 7.65-7.45 (5H, m), 7.39 (2H, d, J=8.5Hz), 7.25-7.08 (3H, m), 4.37 (1H, m), 4.25-4.05 (2H, m), 3.08 (2H, d, J=7Hz), 0.99 (3H, d, J=6.5Hz), 0.84 (3H, d, J=6.5Hz).

Example 25

2-methoxy-4-[2-(N-isopropyl-phenylsulfonylamino)-5-trifluoromethylphenoxymethyl]benzoic acid

[0434]



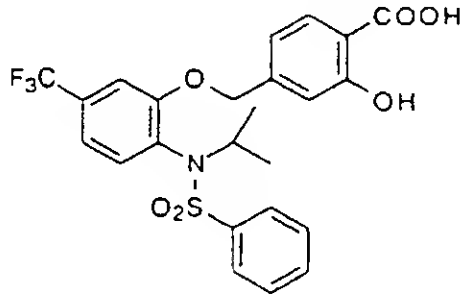
[0435] By using 2-(N-isopropyl-phenylsulfonylamino)-5-trifluoromethylphenol (prepared in Reference Example 24.), the title compound having the following physical data was obtained by the same procedure as Reference Example 6→Example 2.

TLC : Rf 0.49 ($CHCl_3$: MeOH = 9 : 1);
NMR : δ 11.0-10.6 (1H, br), 8.21 (1H, d, J=7.8Hz), 7.9-7.8 (2H, m), 7.71 (1H, d, J=0.6Hz), 7.7-7.4 (3H, m), 7.3-7.2 (2H, m), 7.2-7.1 (1 H, m), 7.00 (1H, d, J=7.8Hz), 5.22 (2H, s), 4.6-4.4 (1H, m), 4.18 (3H, s), 1.08 (3H, d, J=6.6Hz), 0.92 (3H, d, J=6.6Hz).

Example 26

2-hydroxy-4-[2-(N-isopropyl-phenylsulfonylamino)-5-trifluoromethylphenoxymethyl]benzoic acid

[0436]



[0437] By using 2-(N-isopropyl-phenylsulfonylamino)-5-trifluoromethylphenol (prepared in Reference Example 24.), the title compound having the following physical data was obtained by the same procedure as Reference Example 6→Reference Example 23→Example 2.

TLC : Rf 0.56 ($CHCl_3$: MeOH : AcOH= 90 : 9 : 1).
NMR : δ 10.51 (1H, s), 7.95 (1H, d, J=8.0Hz), 7.9-7.8 (2H, m), 7.6-7.4 (3H, m), 7.3-7.2 (3H, m), 7.1-7.0 (2H, m),

5.05 (2H, s), 4.5-4.3 (1H, m), 1.09 (3H, d, J=5.0Hz), 1.06 (3H, d, J=5.0Hz).

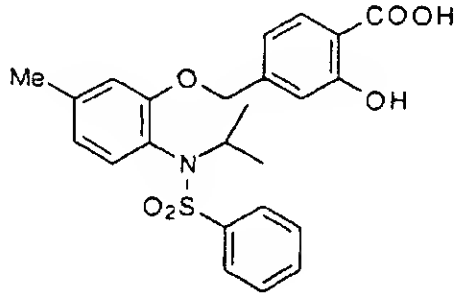
Example 26(1)-26(2)

[0438] By using the corresponding compounds, the title compounds having the following physical data were obtained by the same procedure as Reference Example 6→Reference Example 23→Example 2.

Example 26(1)

2-hydroxy-4-[2-(N-isopropyl-phenylsulfonylamino)-5-methylphenoxymethyl]benzoic acid

[0439]

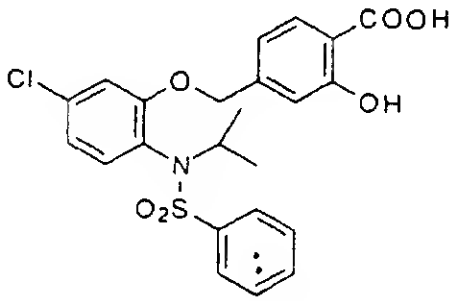


TLC : Rf 0.20 ($CHCl_3$: MeOH = 17 : 3);
NMR : δ 10.50 (1H, s), 7.92 (1H, d, J=8.5Hz), 7.83 (2H, m), 7.54-7.32 (3H, m), 7.05-6.93 (3H, m), 6.81-6.72 (2H, m), 4.97 (2H, s), 4.42 (1H, m), 2.35 (3H, s), 1.13-0.98 (6H, m).

Example 26(2)

2-hydroxy-4-[2-(N-isopropyl-phenylsulfonylamino)-5-chlorophenoxymethyl]benzoic acid

[0440]

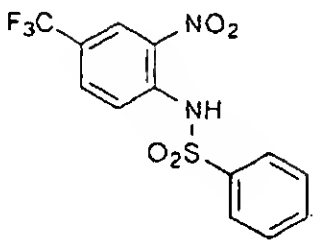


TLC : Rf 0.21 ($CHCl_3$: MeOH = 9 : 1);
NMR : δ 7.93 (1H, d, J=8.0Hz), 7.9-7.7 (2H, m), 7.6-7.3 (3H, m), 7.1-6.9 (5H, m), 4.97 (2H, s), 4.5-4.3 (1H, m), 3.0-2.0 (2H, br), 1.07 (3H, d, J=6.2Hz), 1.04 (3H, d, J=6.2Hz).

Reference Example 25

4-phenylsulfonylamino-3-nitrobenzotrifluoride

[0441]



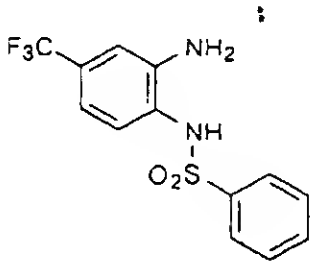
[0442] To a solution of 4-amino-3-nitrobenzotrifluoride (3.09 g) in THF sodium hydride (660 mg) was added. The mixture was stirred for 30 minutes at room temperature. After stirring, benzenesulfonylchloride (3.18 g) was added thereto. The mixture was stirred for 2 hours at room temperature. In addition, sodium hydride (420 mg) was added thereto. The mixture was stirred for 1 hour. The reaction mixture was acidified by adding an equeous solution of ammonium chloride and extracted with ethyl acetate. The organic layer was washed, dried over, filtered and concentrated to give the title compound (4.86 g) having the following physical data.

TLC : Rf 0.31 (hexane : AcOEt = 3 : 1).

Reference Example 26

4-phenylsulfonylamino-3-aminobenzotrifluoride

[0443]



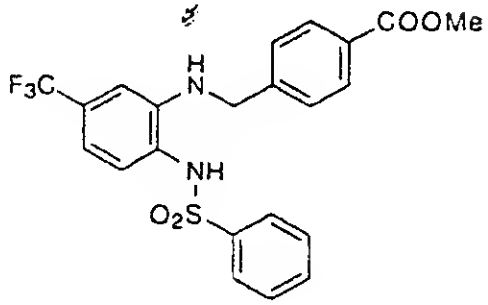
[0444] By using 4-phenylsulfonylamino-3-nitrobenzotrifluoride (2.4 g; prepared in Reference Example 25.), the title compound (1.7 g) having the following physical data was obtained by the same procedure as Reference Example 12.

TLC : Rf 0 17 (hexane : AcOEt = 3 : 1).

Example 27

Methyl 4-(2-phenylsulfonylamino-5-trifluoromethylphenylaminomethyl)benzoate

[0445]



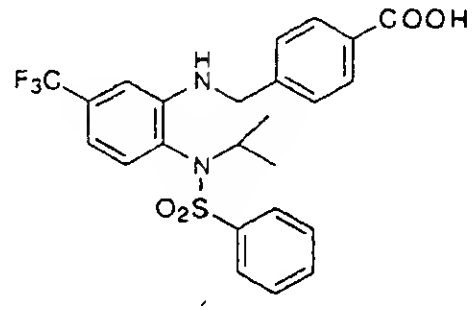
[0446] To a solution of 4-phenylsulfonylamino-3-aminobenzotrifluoride (100 mg; prepared in Reference Example 26.) and terephthal aldehyde acid methyl ester (78 mg) in MeOH (2 ml), acetic acid (1.5 ml) was added. The mixture was stirred for 2 hours at room temperature. After stirring, a solution of sodium cyanoborohydride (30 mg) in MeOH (2 ml) was added. The mixture was stirred for 2 hours at room temperature. The reaction solution was extracted with H_2O-AcOEt, washed, dried over, filtered and concentrated. The precipitate was washed with hexane to give the title compound (146 mg) having the following physical data.

TLC : Rf 0.27 (hexane : AcOEt = 2 : 1);
NMR : δ 8.02 (2H, m), 7.76 (2H, m), 7.6-7.4 (5H, m), 6.74-6.70 (2H, m), 6.55-6.50 (1H, m), 6.02 (1H, bs), 5.35 (1H, m), 4.40 (2H, m), 3.92 (3H, s).

Example 28

4-[2-(N-isopropyl-phenylsulfonylamino)-5-trifluoromethylphenylaminomethyl]benzoic acid

[0447]



[0448] By using methyl 4-(2-phenylsulfonylamino-5-trifluoromethylphenylaminomethyl)benzoate (prepared in Example 27.), the title compound having the following physical date was obtained by the same procedure as Example 17→Example 2.

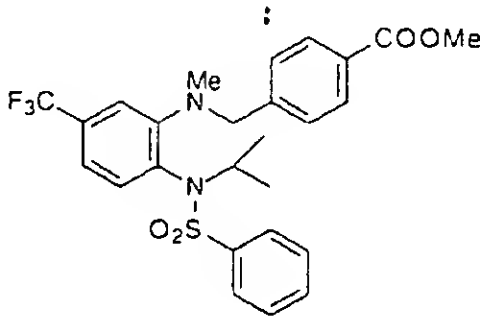
TLC : Rf 0.45 (hexane : AcOEt = 1 : 1);

NMR : δ 8.10 (2H, d, J=8.5 Hz), 7.8-7.7 (2H, m), 7.6-7.4 (5H, m), 6.8-6.7 (2H, m), 6.7-6.6 (1H, m), 5.34 (1H, m), 4.69 (1H, sept, J=7 Hz), 4.45 (2H, d, J=6 Hz), 1.15 (3H, d, J=7Hz), 1.01 (3H, d, J=7Hz).

Example 29

Methyl 4-[N-methyl-[2-(N-isopropyl-phenylsulfonylamino)-5-trifluoromethylphenyl]aminomethyl]benzoate

[0449]



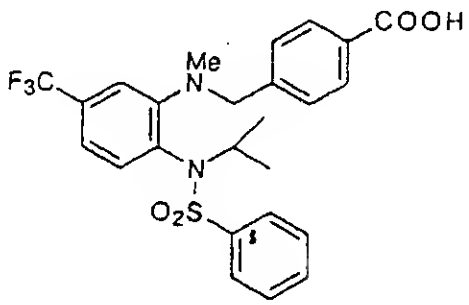
[0450] Methyl 4-[2-(N-isopropyl-phenylsulfonylamino)-5-trifluoromethylphenylaminomethyl]benzoate (200 mg) prepared by the same procedure as Example 17 by using methyl 4-(2-phenylsulfonylamino-5-trifluoromethylphenylaminomethyl)benzoate (prepared in Example 27.) was dissolved in DMF (5 ml). Sodium hydride (64 mg) and methyl iodide (200 ml) were added thereto. The mixture was stirred for 24 hours at 60°C. The reaction mixture was extracted with H_2O-AcOEt, washed, dried over, filtered and concentrated under the reduced pressure. The residue was purified on silica gel column chromatography (hexane : AcOEt = 5 : 1) to give the title compound (105 mg) having the following physical data.

TLC : Rf 0.54 (CH_2Cl_2);
NMR : δ 8.0 (2H, m), 7.9 (2H, m), 7.6-7.5 (3H, m), 7.4 (2H, m), 7.4-7.2 (2H, m), 7.0 (1H, m), 4.6-4.3 (2H, m), 3.92 (3H, m), 2.72 (3H, s), 1.2 (3H, m), 0.8 (3H, m).

Example 30

4-[N-methyl-[2-(N-isopropyl-phenylsulfonylamino)-5-trifluoromethylphenyl]aminomethyl]benzoic acid

[0451]



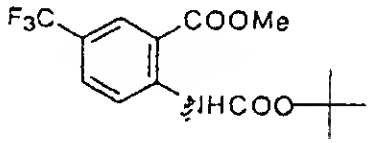
[0452] By using methyl 4-[N-methyl-[2-(N-isopropyl-phenylsulfonylamino)-5-trifluoromethylphenyl]aminomethyl]benzoate (prepared in Example 29.), the title compound having the following physical data was obtained by the same procedure as Example 2.

TLC : Rf 0.45 (hexane : AcOEt = 1 : 1);
NMR : δ 8.09 (2H, d, J=8 Hz), 7.9 (2H, m), 7.7-7.4 (5H, m), 7.2 (2H, m), 7.0 (1H, m), 4.6-4.4 (3H, m), 2.75 (3H, s), 1.26 (3H, d, J=7Hz), 0.85 (3H, d, J=7Hz).

Reference Example 27

Methyl 2-t-butoxycarbonylamino-5-trifluoromethylbenzoate

[0453]



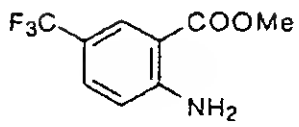
[0454] 4-t-butoxycarbonylaminobenzotrifluoride (3.90 g) was dissolved in THF. At -50°C, t-butyl lithium (30 ml) was edded dropwise thereto. The mixture was stirred for 3 hours with keeping et -50°C. Carbon dioxide ges wes bubbled into this mixture under stirring (the temperature increased to about -30°C.). The solvent was distilled out. The back-extractraction of the residue with 2N NaOH-ether mixture solution was carried out. The aqueous layer was acidified by adding 2N HCl, extracted with ether, washed and dried over. In addition, the layer conteining ether was washed, dried over, filtered and concentreted after combining the said leyer containing ether to give the crude compound. Such crude compound was dissolved in ether. A solution of diazomethane in ether was added thereto until the reaction solution became yellow. The reaction solution was concentrated and purified on silica gel column chromatography (hexane : AcOEt = 20 · 1 10 · 1) to give the title compound (3.80 g) heving the following physical deta.

TLC . Rf 0.70 (hexane : AcOEt = 3 : 1).

Reference Example 28

Methyl 2-amino-5-trifluoromethylbenzoate

[0455]



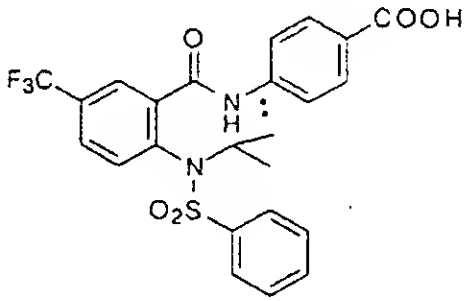
[0456] To a solution of methyl 2-t-butoxycarbonylamino-5-trifluoromethylbenzoate (3.80 g; prepared in Reference Example 27.) in methylene chloride (30 ml), trifluoroacetic acid (6 ml) was added. The mixture was stirred for 8 hours at room temperature. The solvent was distilled off azeotropically with toluene three times. To the reaction mixture, an equeous sodium hydrogencerbonate solution was edded to neutrelize. The mixture was extracted with ethyl acetate, washed, dried, filtered and concentrated under the reduced pressure. The residue was purified on silica get column chromatography (hexane : AcOEt = 5 : 1) to give the title compound (2.35 g) having the following physical data.

TLC : Rf 0.20 (hexane : AcOEt = 5 : 1).

Example 31

4-[2-(N-isopropyl-phenylsulfonylamino)-5-trifluoromethylbenzoylamino]benzoic acid

[0457]



[0458] By using methyl 2-amino-5-trifluoromethylbenzoate (prepared in Reference Example 28.), the title compound having the following physical data was obtained by the same procedure as Reference Example 2→Reference Example 3→Example 1→Example 2

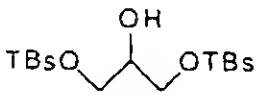
TLC : Rf 0.25 (hexane . AcOEt = 1 : 2);
NMR: δ 10.01 (1H, s), 8.18-8.14 (3H, m), 7.93 (8H, m), 6.64 (1H, d, J=8Hz), 4.67 (1H, sept., J=6.5Hz), 1.09 (3H, d, J=6.5Hz), 0 86 (3H, d, J=6.5Hz).

Reference Example 29

Methyl 4-[2-[N-[1,3-bis(t-butyldimethylsilyloxy)prop-2-yl]-phenylsulfonylamino]-5-trifluoromethylphenoxymethyl]benzoate

(a) 1,3-diOTBs having compound (intermediate)

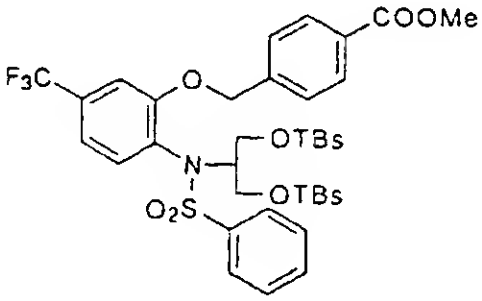
[0459]



[0460] To e solution of glycerol (2 g) in DMF (15 ml), solution of t-butyldimethylsilylchloride (6.5 g) and imidazole (3.3 g) in DMF (8 ml) was added dropwise slowly at 0°C. The solution was stirred for 3 hours at room temperature. The reaction mixture was poured into water, extracted with AcOEt-hexane (AcOEt : hexane = 1 : 1) mixture solution and purified on silica gel column chromatography to give the 1,3-diOTBs having compound (5.8 g) having the following physical date. TLC : Rf 0. 5 (hexane : AcOEt = 9 : 1).

(b) title compound

[0461]



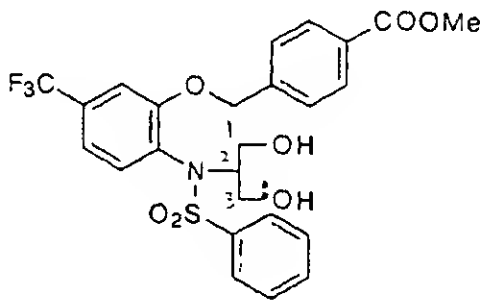
[0462] By using methyl 4-(2-phenylsulfonylamino-5-trifluoromethylphenoxymethyl)benzoate (180 mg; prepared in Example 15.) and the 1,3-diOTBS having compound prepared in the above (a) (247 mg), the title compound (200 mg) having the following physical data was obtained by the same procedure as Example 19.

TLC · Rf 0. 28 (hexane : AcOEt = 9 : 1).

Example 32

Methyl 4-[2-[N-(1,3-dihydroxyprop-2-yl)-phenylsulfonylamino]-5-trifluoromethylphenoxymethyl]benzoate

[0463]



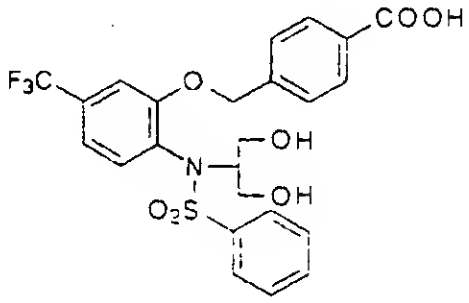
[0464] To a solution of methyl 4-[2-[N-[1,3-bis(t-butyldimethylsilyloxy)prop-2-yl]-phenylsulfonylamino]-5-trifluoromethylphenoxymethyl]benzoate (200 mg; prepared in Reference Example 29.) in THF (3 ml), a solution of tetrabutylanmonimu fluoride (0.57 ml) in THF (1M) was added. The solution was stirred for 3 hours at room temperature. To the reaction compound, water was added. The mixture was extracted with ethyl acetate, washed, dried over and purified on silica gel column chromatography (110 mg) having the following physical data.

TLC : Rf 0.50 (CH_2Cl_2 : MeOH = 9 : 1);
NMR : δ 8.08 (2H, d, J=8.2Hz), 7.78 (2H, d, J=7.2Hz), 7.70-7.24 (8H, m), 5.14 (1H, d, J=12.0Hz), 5.06 (1H, d, J=12.0Hz), 4.50-4.30 (1H, m), 3.93 (3H, s), 3.80-3.20 (4H, m), 2.72 (1H, dd, J=3.6, 18.2Hz).

Example 33

4-[2-[N-(1,3-dihydroxyprop-2-yl)-phenylsulfonylamino]-5-trifluoromethylphenoxymethyl]benzoic acid

[0465]



[0466] By using methyl 4-[2-[N-(1,3-dihydroxyprop-2-yl)-phenylsulfonylamino]-5-trifluoromethylphenoxymethyl]benzoate (prepared in Example 32.), the title compound having the following physical data was obtained by the same procedure as Example 2.

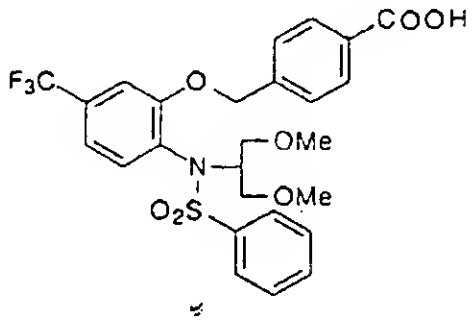
TLC : Rf 0.51 (AcOEt : AcOH= 99 : 1);
NMR: δ 8.13 (2H, d, J=8.4Hz), 7.8-7.7 (2H, m), 7.6-7.2 (8H, m), 5.17 (1H, d, J=11.4Hz), 5.08 (1H, d, J=11.4Hz),

4.5-4.3 (1H, m), 3.6-3.5 (2H, m), 3.4-3.2 (2H, m).

Example 34

4-[2-[N-(1,3-dimethoxyprop-2-yl)-phenylsulfonylamino]-5-trifluoromethylphenoxymethyl]benzoic acid

[0467]



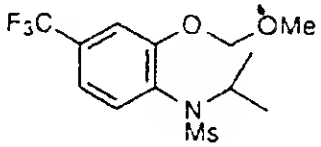
[0468] By using methyl 4-[2-[N-(1 ,3-dihydroxyprop-2-yl)-phenylsulfonylamino]-5-trifluoromethylphenoxymethyl]benzoate (prepared in Exampla 32.), the title compound having the following physical data was obtained by the came procedure as Reference Example 19→Example 2.

TLC : Rf 0.57 ($CHCl_3$: MeOH = 9 : 1);
NMR : δ 8.18 (2H, d, J=8.2Hz), 7.8-7.7 (2H, m), 7.63 (2H, d, J=8.2Hz), 7.6-7.4 (3H, m), 7.3-7.2 (3H, m),5.18 (2H, s), 4.5-4.4 (1H, m), 3.7-3.6 (1H, m), 3.5-3.0 (3H, m), 3.09 (3H, s), 3.04 (3H, s).

Reference Example 30

2-(N-isopropyl-methylsulfonylamino)-5-trifluoromethylphenyl methoxymethyl ether

[0469]



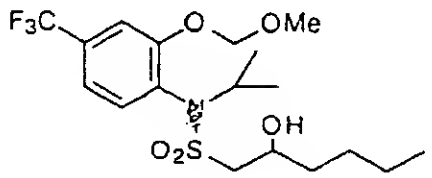
[0470] By using 2-emino-5-trifluoromethylphenyl methoxymethyl ether and mesylchloride, the title compound having the following physical data was obtained by the same procedure as Reference Example 2→Example 17.

TLC : Rf 0.40 (hexane : AcOEt = 2 : 1).

Reference Example 31

2-(N-isopropyl-2-hydroxyhexylsulfonylamino)-5-trifluoromathylphanyl mathoxymathyl athar

[0471]



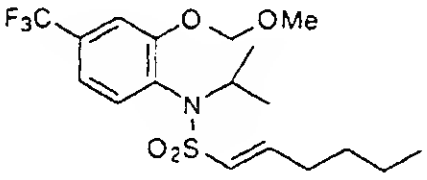
[0472] To a solution of 2-(N-isopropyl-methylsulfonylamino)-5-trifluoromethylphenyl methoxymethyl ether (135 mg; prepered in Reference Example 30.) in THF (3.0 ml), hexamethylphosphoremide (420 ml) was added in a stream of argon. At -78°C, n-butyl lithium (742 ml) was added dropwise thereto. The mixture was stirred for 1.5 hours. To the mixture, a solution of valeraldehyde (102 mg) in THF (1.0 ml) was added dropwisa. The mixture was stirred for 30 minutes. To the reaction mixture, water was added. The mixture was extracted with ethyl acetate, washed, dried over and concentrated with the reduced pressure. The residue was purified on silica gel column chromatography (hexane : AcOEt = 4 : 1) to give the title compound (69 mg) having the following physical data.

TLC : Rf 0.49 (hexane : AcOEt = 2 : 1).

Reference Example 32

2-(N-isopropyl-1-hexenylsulfonylamino)-5-trifluoromethylphenyl methoxymethyl ether

[0473]



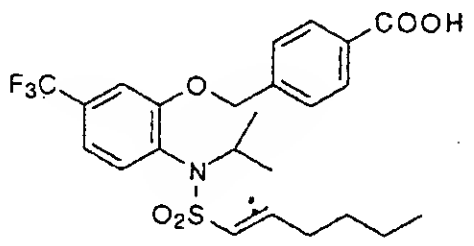
[0474] To a solution of 2-(N-isopropyl-2-hydroxyhexylsulfonylamino)-5-trifluoromethylphenyl methoxymethyl ether (160 mg. prapared in Referance Example 31.) in methylena chlorida (2.0 ml), triethylamine(104 ml) and mesylchlorida (35 ml) were added in a stream of argon at 0°C. The mixture was stirred for 10 minutes. To the mixture, 1,5-diazabicyclo[5.4.0]undecene (134 ml) wes added. The mixture was stirred for 2 hours at room tempereture. To the reaction mixture, diluted HCl was added. The mixture was extracted with ethyl acetate, washed, dried over and concentrated with the reduced pressura. Tha residua was purified on silica gal column chromatography (hexana : AcOEt = 8 : 1) to giva the title compound (140 mg) having the following physical data

TLC : Rl 0.37 (hexane : AcOEt = 3 : 1).

Example 35

4-[2-(N-isopropyl-1-hexenylsulfonylamino)-5-trifluoromethylphenoxymethyl]benzoic acid

[0475]



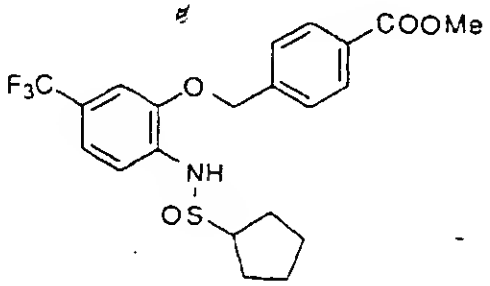
[0476] By using 2-(N-isopropyl-1-hexenylsulfonylamino)-5-trifluoromethylphenyl methoxymethyl ether (prepared in Reference Example 32.), the title compound having the following physical data was obtained by the same procedure as Reference Example 23→Reference Example 6→Exemple 2.

TLC : Rf 0.44 ($CHCl_3$: MeOH : AcOH= 100 : 5 : 1);
NMR : δ 8.19 (2H, d, J=8.2Hz), 7.62 (2H, d, J=8.2Hz), 7.22-7.45 (3H, m), 6.68 (1H, td, J=7.0, 15.0Hz), 6.09 (1H, td, J=1.4, 15.0Hz), 5.19 (2H, s), 4.15 (1H, m), 1.97 (2H, m), 1.16-1.40 (7H, m), 1.03 (3H, d, J=6.8Hz), 0.86 (3H, m).

Reference Example 33

Methyl 4-(2-cyclopentylsulfinylamino-5-trifluoromethylphenoxymethyl)benzoate

[0477]



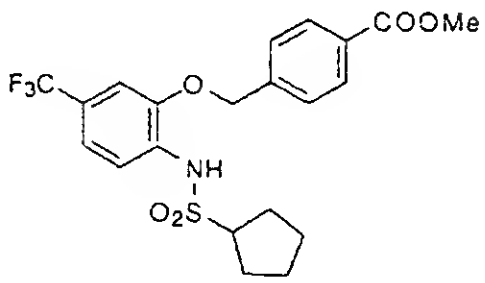
[0478] To a solution of methyl 4-(2-amino-5-trifluoromethylphenoxymethyl)benzoate (300 mg) in methylene chloride (3.0 ml), pyridine (187 ml) and triphenylphosphine (315 mg) were added in e stream of ergon. At 0^C, cyclopentylsulfonylchloride (202 mg) was added dropwise thereto. The mixture wes stirred for 6 hours et room temperature. To the reaction mixture water was added. The mixture was extracted with ethyl acetate, washed, dried over and concentrated with lhe reduced pressure. The residue was purified on silica gel column chromatography (hexane : AcOEt = 2 : 1 1 : 1) to give the title compound (309 mg) heving the following physical deta.

TLC : Rf 0.23 (hexane : AcOEt = 2 : 1).

Example 36

Methyl 4-(2-cyclopentylsulfonylamino-5-trifluoromethylphenoxymethyl)benzoate

[0479]



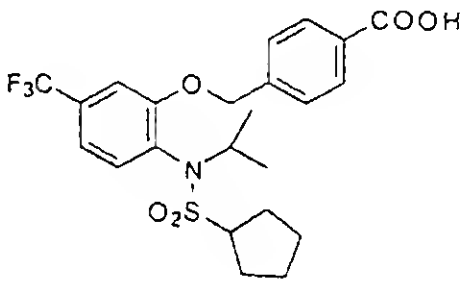
[0480] To a solution of methyl 4-(2-cyclopentylsulfinylamino-5-trifluoromethylphenoxymethyl)benzoate (305 mg; prepared in Reference Example 33.) in methylene chloride (4.0 ml), meta-chloroperbenzoic acid (456 mg) was added at 0°C. The mixture was stirred for 1 hour. The reaction mixture was diluted with ethyl acetate, washed, dried over and concentrated under the reduced pressure to give the title compound (317 mg) having the following physical data.

TLC : Rf 0.56 (hexane : AcOEt = 2 : 1);
NMR : δ 8.11 (2H, d, J=8.6Hz), 7.73 (1H, brd, J=9.0Hz), 7.47 (2H, d, J=8.6Hz), 7.25 (1H, m), 7.15 (1H, d, J=1.4Hz), 6.95 (1H, brs), 5.21 (2H, s), 3.95 (3H, s), 3.54 (1H, m), 1.53-2.16 (8H, m).

Example 37

4-[2-(N-isopropyl-cyclopentylsulfonylamino)-5-trifluoromethylphenoxymethyl]benzoic acid

[0481]



[0482] By using methyl 4-(2-cyclopentylsulfonylamino-5-trifluoromethylphenoxymethyl)benzoate (prepared in Example 36.), the title compound having the following physical deta was obtained by the same procedure es Example 17→Example 2.

TLC : Rf 0.40 ($CHCl_3$: MeOH : AcOH= 100 : 5 : 1);
NMR : δ 8.17 (2H, d, J=8.4Hz), 7.61 (2H, d, J=8.4Hz), 7.38 (1H, d, J=8.0Hz), 7.28 (2H, m), 5.17 (2H, s), 4.36 (1H, sept, J=6.6Hz), 3.51 (1H, m), 1.84-2.10 (3H, m), 1.61-1.84 (3H, m), 1.30-1.56 (2H, m), 1.24 (3H, d, J=6.6Hz), 1.08 (3H, d, J=6.6Hz).

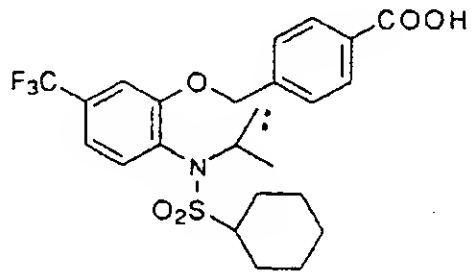
Example 37(1)-37(7)

[0483] By using the corresponding compounds, the title compounds having the following physical data wer obtained by the same procedure as Reference Example 33→Example 36→Example 17→Example 2.

Example 37(1)

4-[2-(N-isopropyl-cyclohexylsulfonylamino)-5-trifluoromethylphenoxymethyl]benzoic acid

[0484]

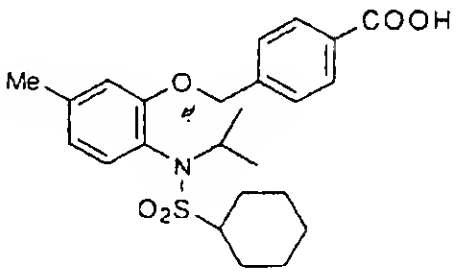


TLC : Rf 0.27 (AcOEt : hexane = 1 : 1);
NMR : δ 8.17 (2H, d, J=8Hz), 7.61 (2H, d, J=8Hz), 7.42 (1H, d, J=8Hz), 7.28 (1H, d, J=8Hz), 7.26 (1H, s), 5.19 (2H, s), 4.32 (1H, m), 2.88 (1H, m), 2.25-2.04 (2H, m), 1.92-1.35 (5H, m), 1.30-0.60 (9H, m).

Exemple 37(2)

4-[2-(N-isopropyl-cyclohexylsulfonylamino)-5-methylphenoxymethyl]benzoic acid

[0485]

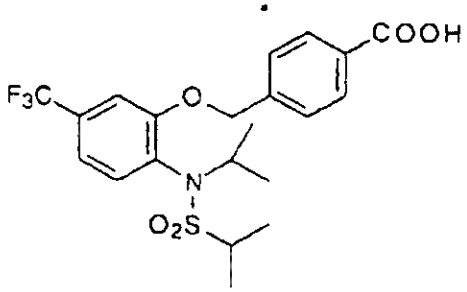


TLC : Rf 0.37 ($CHCl_3$: MeOH : AcOH= 100 : 5 : 1),
NMR : δ 8.15 (2H, d, J=8.6Hz), 7.59 (2H, d, J=8.6Hz), 7.17 (1H, d, J=8.4Hz), 6.82 (2H, m), 5.13 (2H, s), 4.32 (1H, m), 2.88 (1H, tt, J=3.2, 12.0Hz), 2.35 (3H, s), 2.15 (2H, m), 1.36-1.90 (5H, m), 1.23 (3H, d, J=6.6Hz), 1.12 (3H, d, J=6.6Hz), 0.82 (1H, m).

Example 37(3)

4-[2-(N-isopropyl-isopropylsulfonylamino)-5-trifluoromethylphenoxymethyl]benzoic acid

[0486]

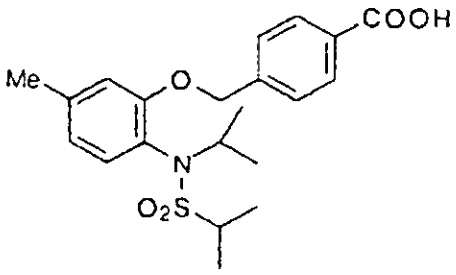


TLC : Rf 0.34 ($CHCl_3$: MeOH : AcOH= 100 : 5 : 1);
NMR : δ 8.18 (2H, d, J=8.4Hz), 7.60 (2H, d, J=8.4Hz), 7.42 (1H, d, J=8.0Hz), 7.23-7.33 (2H, m), 5.17 (2H, s), 4.32 (1H, sept, J=6.6Hz), 3.17 (1H, sept, J=7.0Hz), 1.32 (3H, d, J=7.0Hz), 1.25 (3H, d, J=6.6Hz), 1.19 (3H, d, J=7.0Hz), 1.09 (3H, d, J=6.6Hz).

Exemple 37(4)

4-[2-(N-isopropyl-isopropylsulfonylamino)-5-methylphenoxymethyl]benzoic acid

[0487]

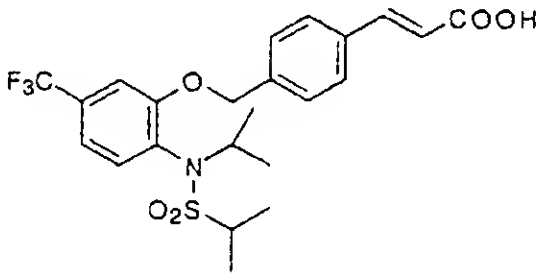


TLC : Rf 0.46 ($CHCl_3$: MeOH : AcOH= 100 : 5 : 1),
NMR : δ 8.15 (2H, d, J=8.2Hz), 7.57 (2H, d, J=8.2Hz), 7.16 (1H, d, J=8.4Hz), 6.81 (2H, m), 5.11 (2H, s), 4.31 (1H, sept, J=6.6Hz), 3 16 (1H, sept, J=6.8Hz), 2.36 (3H, s), 1.31 (3H, d, J=6.8Hz), 1.23 (3H, d, J=6.6Hz), 1.18 (3H, d, J=6.6Hz), 1.08 (3H, d, J=6.8Hz).

Example 37(5)

4-[2-(N-isopropyl-isopropylsulfonylamino)-5-trifluoromethylphenoxymethyl]cinnamic acid

[0488]

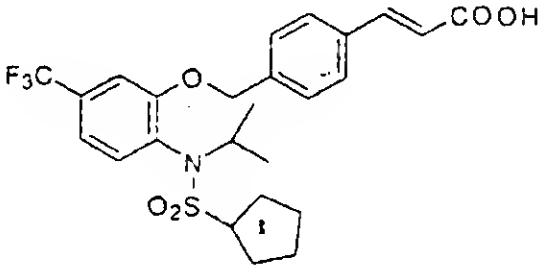


TLC : Rf 0.20 (AcOEt : hexane = 1 : 1);
NMR : δ 7.79 (1H, d, J=15Hz), 7.61 (2H, d, J=8Hz), 7.50 (2H, d, J=8Hz), 7.40 (1H, d, J=8Hz), 7.34-7.20 (2H, m), 6.48 (1H, d, J=15Hz), 5.12 (2H, s), 4.31 (1H, m), 3.14 (1H, m), 1.31 (3H, d, J=7Hz), 1.25 (3H, d, J=7Hz), 1.15 (3H, d, J=7Hz), 1.07 (3H, d, J=7Hz).

Example 37(6)

4-[2-(N-isopropyl-cyclopentylsulfonylamino)-5-trifluoromethylphenoxymethyl]cinnamic acid

[0489]

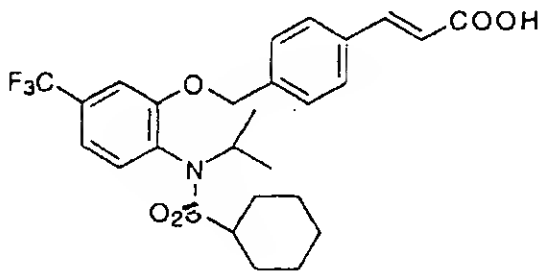


TLC : Rf 0.24 (AcOEt : hexane = 1 : 1);
NMR : δ 7.80 (1H, d, J=15Hz), 7.61 (2H, d, J=8Hz), 7.53 (2H, d, J=8Hz), 7.38 (1H, d, J=8Hz), 7.30-7.22 (2H, m), 6.48 (1H, d, J=15Hz), 5.13 (2H, s), 4.35 (1H, m), 3.49 (1H, m), 2.20-1.16 (11H, m), 1.07 (3H, d, J=7Hz).

Example 37(7)

4-[2-(N-isopropyl-cyclohexylsulfonylamino)-5-trifluoromethylphenoxymethyl]cinnamic acid

[0490]

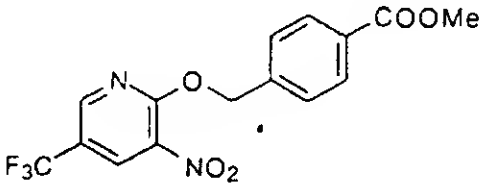


TLC : Rf 0.27 (AcOEt : hexane = 1 : 1);
NMR : δ 7.80 (1H, d, J=15Hz), 7.61 (2H, d, J=8Hz), 7.52 (2H, d, J=8Hz), 7.41 (1H, d, J=8Hz), 7.34-7.20 (2H, m), 6.48 (1H, d, J=15Hz), 5.13 (2H, s), 4.32 (1H, m), 2.87 (1H, m), 2.21-2.00 (2H, m), 1.90-1.34 (5H, m), 1.26 (3H, d, J=7Hz), 1.18-0.60 (6H, m).

Reference Example 34

Methyl 4-(3-nitro-5-trifluoromethylpyridine-2-yloxymethyl)benzoate

[0491]



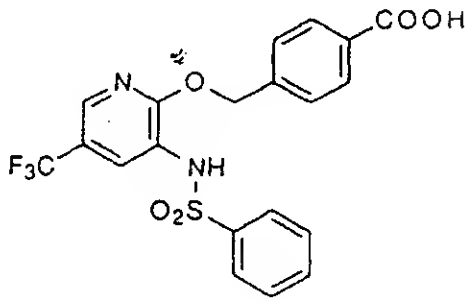
[0492] To a solution of 2-hydroxy-3-nitro-5-trifluoromethylpyridine (1.0 g) in toluene (10 ml), methyl 4-chloromethylbenzoate (1.32 g) and silver oxide (1.23 g) were added in a stream of argon. The mixture was refluxed for 18 hours with heating. The reaction mixture was filtered. The filtrate was concentrated. The residue was recrystallized from ethyl acetate to give the title compound (982 mg) having the following physical data.

TLC : Rf 0.34 (hexane : AcOEt = 3 : 1)

Example 38

4-(3-phenylsulfonylamino-5-trifluoromethylpyridine-2-yloxymethyl)benzoic acid

[0493]



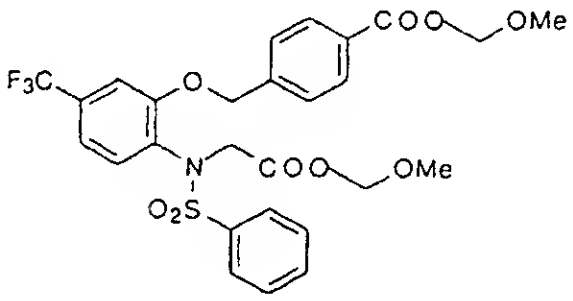
[0494] By using methyl 4-(3-nitro-5-trifluoromethylpyridine-2-yloxymethyl)benzoate (prepared in Reference Example 34.), the title compound having the following physical data was obtained by the same procedure as Reference Example 12→Reference Example 2→Example 2.

TLC : Rf 0.50 ($CHCl_3$: MeOH : AcOH= 100 : 5 : 1);
NMR (DMSO-d_6) : δ 12.94 (1H, m), 10.46 (1H, m), 8.33 (1H, m), 7.89 (2H, d, J=8.4Hz), 7.85 (1H, d, J=2.2Hz), 7.73 (2H, m), 7.43-7.65 (3H, m), 7.36 (2H, d, J=8.4Hz), 5.33 (2H, s).

Reference Example 35

4-[2-(N-methoxymethoxycarbonylmethyl-phenylsulfonylamino)-5-trifluoromethylphenoxymethyl]benzoic acid • methoxymethyl ester

[0495]



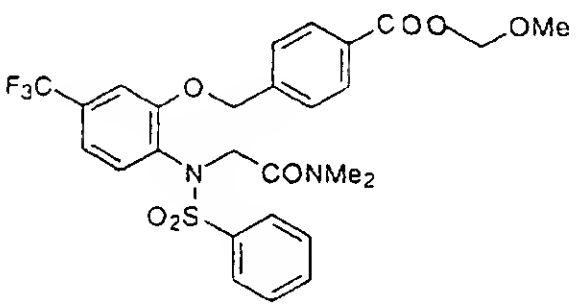
[0496] 4-[2-(N-carboxymethyl-phenylsulfonylamino)-5-trifluoromethylphenoxymethyl]benzoic acid (446 mg) prepared by the same procedure as Example 17→Example 2 by using methyl 4-(2-phenylsulfonylamino-5-trifluoromethylphenoxymethyl)benzoate (prepared in Example 15.) was dissolved in DMF (5 ml). To the solution, methoxymethyl chloride (160 ml) and triethylamine(300 ml) were added dropwise. The mixture was stirred for 2 hours at room temperature. Water was added thereto. The mixture was extracted with ethyl acetate, washed, dried over, filtered and concentrated to give the title compound (476 mg) having the following physical data.

TLC : Rf 0.20 (hexane : AcOEt = 3 : 1).

Reference Example 36

4-[2-[N-(N,N-dimethylaminocarbonylmethyl)-phenylsulfonylamino]-5-trifluoromethylphenoxymethyl]benzoic acid · methoxymethyl ester

[0497]



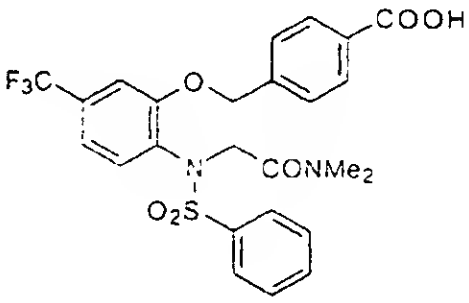
[0498] To a solution of 4-[2-(N-methoxymethoxycarbonylmethyl-phenylsulfonylamino)-5-trifluoromethylphenoxymethyl]benzoic acid · methoxymethyl ester (476 mg; prepared in Reference Example 35.) in THF (2 ml), dimethylamine(0.8 ml) was added. The mixture was stirred for 3 days at room temperature. The solvent was distilled off. The residue was purified on silica gel column chromatography (hexane : AcOEt = 2 : 1 1 : 1) to give the title compound (290 mg) having the following physical data.

TLC : Rf 0.26 (hexane : AcOEt = 1 : 1).

Example 39

4-[2-[N-(N,N-dimethylaminocarbonylmethyl)-phenylsulfonylamino]-5-trifluoromethylphenoxymethyl]benzoic acid

[0499]



[0500] By using 4-[2-[N-(N,N-dimethylaminocarbonylmethyl)-phenylsulfonylamino]-5-trifluoromethylphenoxymethyl]benzoic acid · methoxymethyl ester (prepared in Reference Example 36.), the title compound having the following physical data was obtained by the same procedure as Reference Example 23.

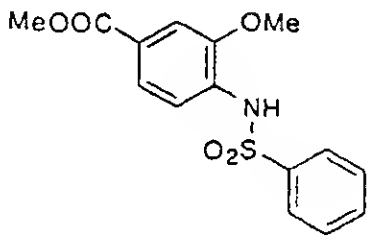
TLC : Rt 0.24 (AcOEt);

NMR : δ 8.10-8.06 (2H, m), 7.71-6.64 (3H, m), 7.55-7.47 (1H, m), 7.42-7.10 (6H, m), 4.94 (2H, s), 4.56 (2H, s), 3.04 (3H, s), 2.86 (3H, s).

Reference Example 37

Methyl 4-phenylsulfonylamino-3-methoxybenzoate

[0501]



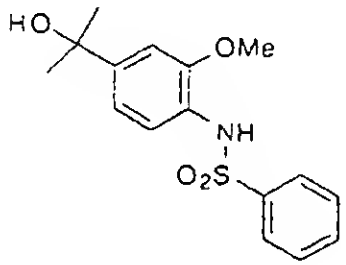
[0502] By using 4-nitro-3-hydroxybenzoic acid, the title compound having the following physical data was obtained by the same procedure as Reference Example 6→Reference Example 12→Reference Example 2.

TLC : Rf 0.12 (hexane : AcOEt = 3 : 1).

Reference Example 38

1-methyl-1-(4-phenylsulfonylamino-3-methoxyphenyl)ethanol

[0503]



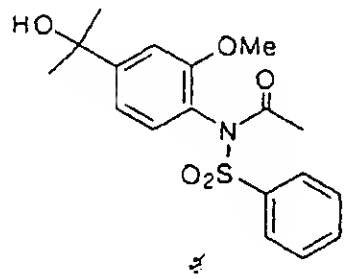
[0504] To a suspension of methyl 4-phenylsulfonylamino-3-methoxybenzoate (3.2 g; prepared in Reference Example 37.) in THF (50 ml), methyl lithium in ether (38.8 ml) was added dropwise at -65°C. The mixture was slowly warmed to 5°C over a period of 3 hours under stirring. The reaction mixture was neutralized by adding diluted HCl and extracted with ethyl acetate. The organic layer was washed, dried over and concentrated to give the title compound having the following physical data.

TLC : Rf 0.18 (hexane : AcOEt = 1 : 1).

Reference Example 39

1-methyl-1-[4-(N-acetyl-phenylsulfonylamino)-3-methoxyphenyl]ethanol

[0505]



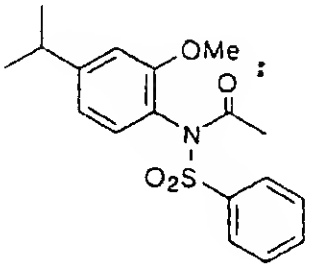
[0506] To a solution of 1-methyl-1-(4-phenylsulfonylamino-3-methoxyphenyl)ethanol (2.65 g; prepared in Reference Example 38.) in methylene chloride (15 ml), acetic anhydride (3.05 ml) and triethylamine (4.60 ml) were added. The mixture was stirred overnight et room temperature. The solvent was distilled off. The residue was purified on silica gel column chromatography (hexane : AcOEt = 3 : 4) to give the title compound (2.33 g) having the following physical data.

TLC : Rf 0.19 (hexene : AcOEt = 1 : 1).

Reference Example 40

2-(N-acetyl-phenylsulfonylamino)-5-isopropylphenyl methyl ether

[0507]

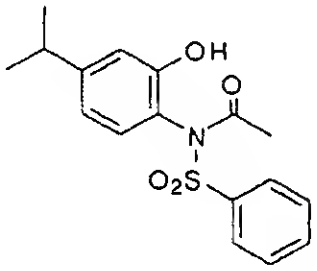


[0508] To a solution of 1-methyl-1-[4-(N-ecetyl-phenylsulfonylemino)-3-methoxyphenyl]ethanol (2.50 g; prepered in Reference Example 39.) in methylene chloride (10 ml), trifluoroacetic acid (10 ml) and triethylsilane (3.3 ml) were added at 0°C. The mixture was stirred for 1 hour at room temperature. The reaction mixture was added to saturated sodium hydrogencarbonate carefully The mixture was extracted with ethyl ecetate. The organic leyer was weshed, dried over end concentrated. The residue was purified on silica gel column chromatography (hexene : AcOEt = 3 : 1) to give the title compound (2.33 g) having the following physical data. TLC : Rf 0.24 (hexane : AcOEt = 1 : 1).

Reference Example 41

2-(N-acetyl-phenylsulfonylamino)-5-isopropylphenol

[0509]



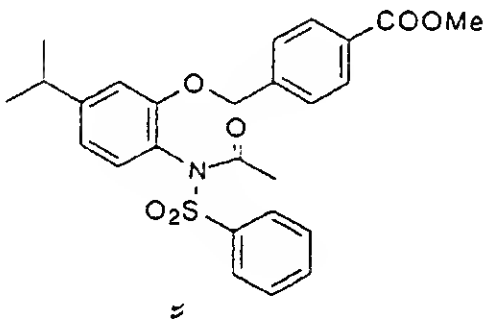
[0510] To a solution of 2-(N-acetyl-phenylsulfonylamino)-5-isopropylphenyl methyl ether (2.28 g; prepared in Reference Example 40.) in methylene chloride (15 ml), boron tribromide (1.36 ml) was added at 0°C. The mixture was stirred for 5 hours at 10°C. The reaction mixture was poured into iced water, extracted with ethyl acetate. The organic layer was washed, dried over and concentrated. The residue was purified on silica gel column chromatography (benzene : AcOEt = 23 : 2) and recrystallized from AcOEt-hexane mixture solution to give the title compound (1.55 g) having the following physical data.

TLC : Rf 0.24 (benzene : AcOEt = 9 : 1).

Reference Example 42

Methyl 4-[2-(N-acetyl-phenylsulfonylamino)-5-isopropylphenoxymethyl]benzoate

[0511]



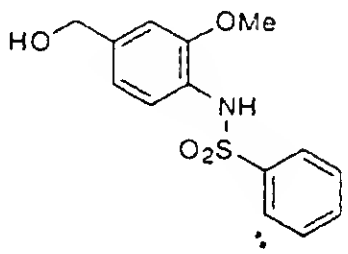
[0512] By using 2-(N-acetyl-phenylsulfonylamino)-5-isopropylphenol (1.50 g; prepared in Reference Example 41.), the title compound (2.22 g) having the following physical data was obtained by the same procedure as Reference Example 6.

TLC Rf 0.24 (hexane : AcOEt = 7 : 3).

Reference Example 43

4-(phenylsulfonylamino)-3-methoxybenzyl alcohol

[0513]



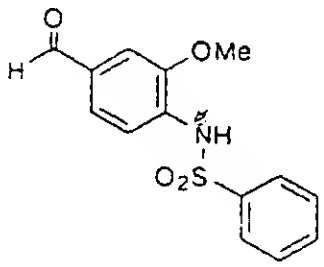
[0514] A solution of methyl 4-phenylsulfonylamino-3-methoxybenzoate (1.5 g; prepared in Reference Example 37.) in THF (90 ml) was cooled to -78°C in a stream of argon. The solution of diisobutylaluminum hydride (1.0 M) in hexane (22 ml) was added dropwise thereto. The mixture was stirred for 4 hours at -78°C. After the temperature increased to room temperature, the mixture was diluted with ether (100 ml). A saturated aqueous sodium sulfate (1.5 ml) was added thereto slowly. The mixture was stirred for 30 minutes, dried over, filtered and concentrated to give the title compound (1.5 g)

TLC : Rf 0.31 (AcOEt : hexane = 2 : 1).

Reference Example 44

4-phenylsulfonylamino-3-methoxybenzaldehyde

[0515]



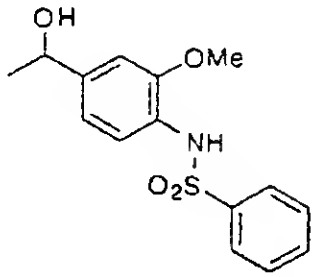
[0516] To a solution of 4-phenylsulfonylamino-3-methoxybenzyl alcohol (522 mg; prepared in Reference Example 43.) in methylene chloride (15 ml), manganese dioxide (3 g) was added in a stream of argon. The solution was stirred for 1 hour at room temperature. After the termination of reaction, the reaction mixture was filtered. The filtrate was concentrated to give the title compound (404 mg) having the following physical data.

TLC : Rf 0.57 (AcOEt : hexane = 3 : 2).

Reference Example 45

1-(4-phenylsulfonylamino-3-methoxyphenyl)ethanol

[0517]



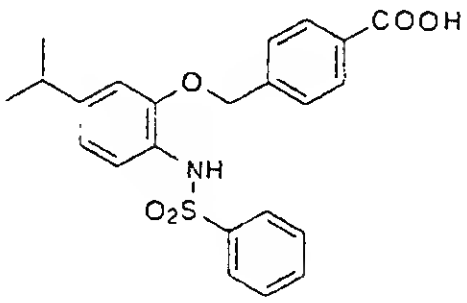
[0518] A solution of 4-phenylsulfonylamino-3-methoxybenzaldehyde (400 mg; prepared in Reference Example 44.) in THF (10 ml) was cooled to at -78°C mg; prepared in Reference Example 44) in THF (10 ml) was cooled to at -78°C in a stream of argon. A solution of methyl lithium (1.0M) in diethyl ether (3.4 ml) was edded dropwise thereto. The mixture was stirred for 20 minutes. After the termination of reaction, a mixture of H_2O + 1N HCl was added thereto to stop the reaction. The mixture was extracted with ethyl acetate three times. The organic layer was washed, dried over and purified on silica gel column chromatography (AcOEt : hexene = 1 : 1) to give the title compound (421 mg) heving the following physical data.

TLC : Rf 0.34 (AcOEt : hexane = 3 : 2).

Example 40

4-(2-phenylsulfonylemino-5-isopropylphenoxymethyl)benzoic acid

[0519]

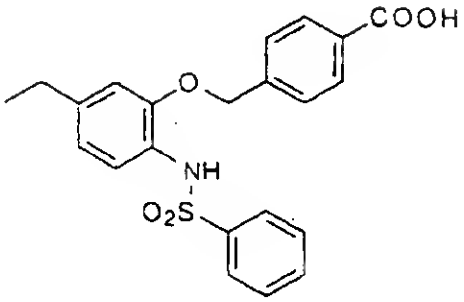


[0520] By using methyl 4-[2-(N-ecetyl-phenylsulfonylamino)-5-isopropylphenoxymethyl]benzoate (2.00 g; prepared in Reference Example 42.), the title compound (1.66 g) having the following physical data was obtained by the same procedure as Example 2.

TLC : Rf 0.49 ($CHCl_3$: MeOH = 4 : 1);
NMR (DMSO-d_6) : δ 7.84 (2H, d, J=8.5Hz), 7.79-7.53 (5H, m), 7.41 (2H, d, J=8.5Hz), 6.90 (1H, d, J=8Hz), 6.63 (1H, d, J=2Hz), 6.55 (1H, dd, J=8 and 2Hz), 4.82 (2H, s), 2.72 (1H, m), 1.10 (6H, d, J=7Hz).

Example 41

[0521]



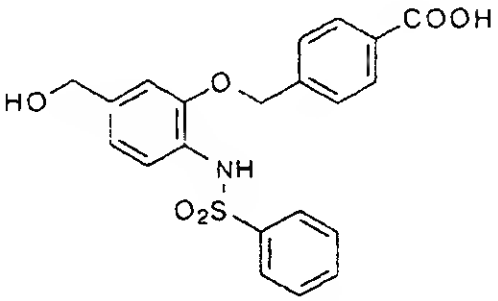
[0522] By using 1-(4-phenylsulfonylamino-3-methoxyphenyl)ethanol (prepared in Reference Example 45.), the title compound having the following physical data was obtained by the same procedure as Reference Example 40 →Reference Example 39→Reference Example 41→Reference Example 6→ Example 2.

TLC : Rf 0.29 (AcOEt : hexane : AcOH= 5 : 14 : 1);
NMR (DMSO-d_6) : δ 12.87 (1H, brs), 9.53 (1H, brs), 7.83 (2H, d, J=8.5Hz), 7.78-7.50 (5H, m), 7.39 (2H, d, J=8.0Hz), 6.86 (2H, d, J=8.0Hz), 6.57 (1H, d, J=2.0Hz), 6.50 (1H, dd, J=8, 2Hz), 4.82 (2H, brs), 2.44 (2H, q, J=7.5Hz), 1.08 (3H, t, J=7.5Hz).

Example 42

4-(2-phenylsulfonylamino-5-hydroxymethylphenoxymethyl)benzoic acid

[0523]



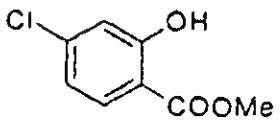
[0524] By using methyl 4-nitro-3-hydroxybenzoate, the title compound having the following physical data was obtained by the same procedure as Reference Example 19→Reference Example 20→Reference Example 2→Reference Example 43→Reference Example 39→Reference Example 23→Reference Example 6→Example 2.

TLC : Rf 0.39 (AcOEt : hexane : AcOH= 13 : 6 : 1);
NMR (DMSO-d_6) : δ 12.83 (1H, brs), 9.56 (1H, s), 7.83 (2H, d, J=8.5Hz), 7.78-7.50 (5H, m), 7.38 (2H, d, J=8.5Hz), 6.88 (1H, d, J=8.0Hz), 6.74 (1H, s), 6.56 (1H, d, J=8.0Hz), 5.10 (1H, brt, J=5.5Hz), 4.83 (2H, s), 4.34 (2H, d, J=5.5Hz).

Reference Example 46

Mathyl 4-chloro-2-hydroxybenzoata

[0525]



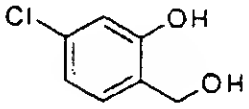
[0526] To a solution of 4-chloro-2-hydroxybenzoic acid (5.0 g) in ether (50 ml), diazomethane in ether was added until the reaction was terminated at 0°C. The reaction mixture was concentrated under the reduced pressure. The residue was purified on silice gel column chromatography (hexane : AcOEt = 4 : 1) to give the title compound (5.4 g) having tha following physical data.

TLC : Rf 0.60 (hexane : AcOEt = 2 : 1).

Reference Example 47

2-hydroxymethyl-5-chlorophenol

[0527]



[0528] To a solution of lithium aluminum hydrida (1.1 g) in THF (50 ml),

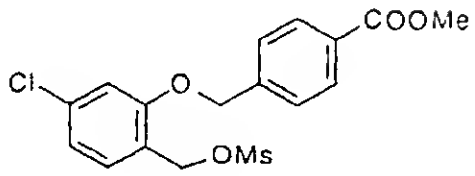
[0529] To a solution of lithium aluminum hydride (1.1 g) in THF (50 ml), methyl 4-chloro-2-hydroxybenzoate (5.38 g; prepared in Reference Example 46.) in THF (50 ml) was added dropwise in a stream of ergon at 0°C. After the solution was warmed to at room temperature, the solution was stirred for 30 minutes. To the reaction mixture, water was added. The mixture was extracted with mixtura solution of ethar-AcOEt, washed, dried over and concentrated undar the reduced pressure. The residue was recrystallized from mixture solution of hexane-AcOEt to give the title compound (3.92 g) having the following physical data.

TLC . Rf 0.60 (hexane : AcOEt = 1 : 1).

Reference Example 48

Methyl 4-(2-mesyloxymethyl-5-chlorophenoxymethyl)benzoate

[0530]



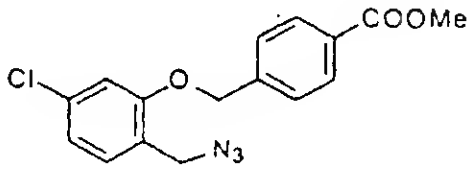
[0531] By using 2-hydroxymethyl-5-chlorophenol (prepared in Reference Example 47.), the title compound having the following physical date was obteined by the same procedure es Reference Example 6→Reference Example 8.

TLC : Rf 0.60 (benzene : acetone = 9 : 1).

Reference Example 49

Methyl 4-(2-azidomethyl-5-chlorophenoxymethyl)benzoate

[0532]



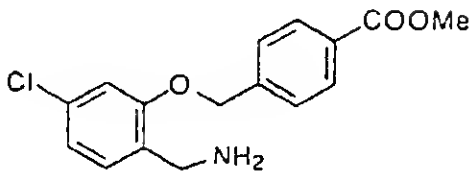
[0533] To a solution of methyl 4-(2-mesyloxymethyl-5-chlorophenoxymethyl)benzoate (628 mg; prepared in Reference Example 48.) in DMF (5.0 ml), sodium azide (530 mg) was added in a stream of argon. The mixture was stirred for 40 minutes at 60°C. The reaction mixture was diluted with ethyl acetate. The impurity was filtered with celite. The filtrate was washed, dried over and concentrated under the reduced pressure. The residue was purified on silica gel column chromatography (hexane : AcOEt = 10 : 1) to give the title compound (404 mg) having the following physical data.

TLC : Rf 0.56 (hexane : AcOEt = 4 : 1).

Reference Example 50

Methyl 4-(2-aminomethyl-5-chlorophenoxymethyl)benzoate

[0534]



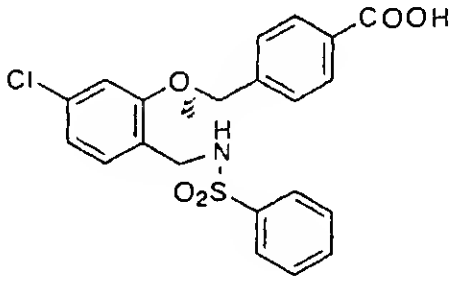
[0535] To a solution of methyl 4-(2-azidomethyl-5-chlorophenoxymethyl)benzoate (389 mg; prepared in Reference Example 49.) in THF (4.0 ml), triphenylphosphine (462 mg) was added at room temperature. The mixture was stirred for 3 hours. After stirring, water was added thereto. The mixture was stirred for 15 hours. The reaction mixture was concentrated under the reduced pressure. The residue was purified on silica gel column chromatography ($CHCl_3$: MeOH = 50 : 1 10 : 1) to give the title compound (339 mg) having the following physical data.

TLC : Rf 0.22 ($CHCl_3$: MeOH = 10 : 1).

Example 43

4-(2-phenylsulfonylaminomethyl-5-chlorophenoxymethyl)benzoic acid

[0536]



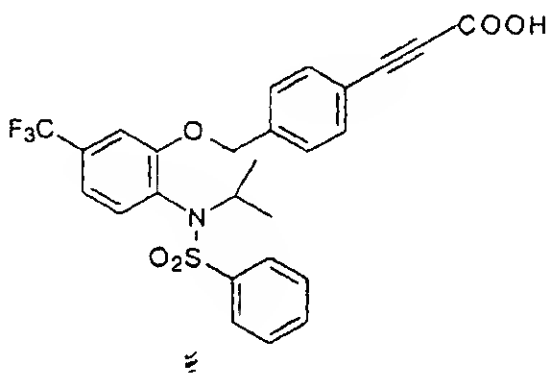
[0537] By using methyl 4-(2-aminomethyl-5-chlorophenoxymethyl)benzoate (prepared in Reference Example 50.), the title compound having the following physical data was obtained by the same procedure as Reference Example 2→Example 2.

TLC . Rf 0.49 ($CHCl_3$: MeOH : AcOH= 100 : 5 : 1);
NMR (DMSO-d_6) : δ 7.94 (2H, d, J=8.0Hz), 7.77 (2H, m), 7.45-7.70 (5H, m), 7.25 (1H, d, J=8.2Hz), 7.05 (1H, d, J=1.8Hz), 6.94 (1H, dd, J=1.8, 8.2Hz), 5.20 (2H, s), 4.00 (2H, s).

Example 44

4-[2-(N-isopropyl-phenylsulfonylamino)-5-trifluoromethylphenoxymethyl]phenylpropiolic acid

[0538]



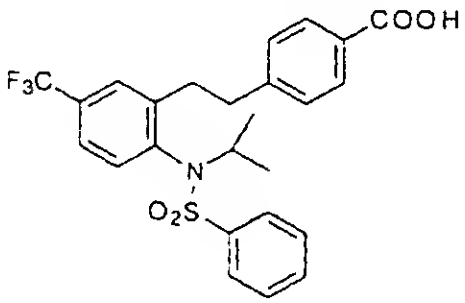
[0539] By using 4-[2-(N-isopropyl-phenylsulfonylamino)-5-trifluoromethylphenoxymethyl]benzoic acid (prepared in Example 18 (9).), the title compound having the following physical data was obtained by the same procedure as Reference Example 13→Reference Example 14→Reference Example 15→Example 2.

TLC : Rf 0.32 ($CHCl_3$: MeOH = 8 : 2);
NMR : δ 7.80 (2H, d, J=8Hz), 7.64 (2H, d, J=8Hz), 7.68-7.26 (8H, m), 5.09 (2H, s), 4.38 (1H, sept, J=6.5Hz), 1.04 (6H, d,J=6.5Hz).

Example 45

4-[2-[2-(N-isopropyl-phenylsulfonylamino)-5-trifluoromethylphenyl]ethyl]benzoic acid

[0540]



[0541] By using methyl 4-[2-(2-t-butoxycarbonylamino-5-trifluoromethylphenyl)-(EZ)-vinyl]benzoate, the title compound having the following physical data was obtained by the same procedure as Reference Example 20→Reference Example 23→Reference Example 2→Example 17→Example 2.

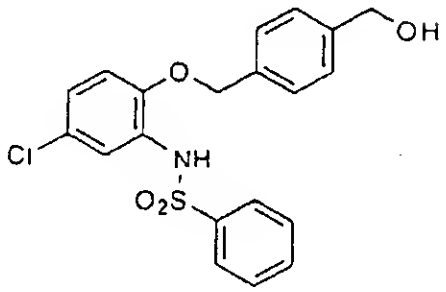
TLC : Rf 0.46 ($CHCl_3$: MeOH = 9 . 1);
NMR : δ 8.09 (2H, d, J=8.2Hz), 7.8-7.7 (2H, m), 7.7-7.3 (7H. m), 6.88 (1H, d, J=8.2Hz), 4.7-4.5 (1H, m), 3.4-3.1

(2H, m), 3.1-2.9 (2H, m), 1.03 (3H, d, J=6.8Hz), 0.93 (3H, d, J=6.8Hz).

Example 46

4-(2-phenylsulfonylamino-4-chlorophenoxymethyl)benzyl alcohol

[0542]



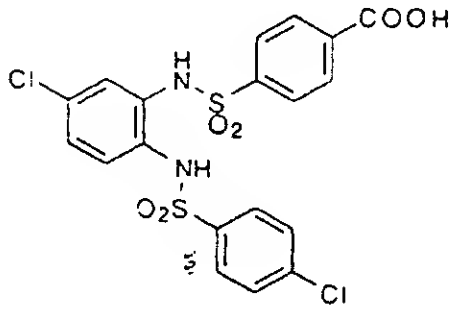
[0543] By using methyl 4-(2-phenylsulfonylamino-4-chlorophenoxymethyl)benzoate (prepared in Example 7 (a).), the title compound having the following physical data was obtained by the same procedure as Reference Example 43.

TLC : Rf 0.24 (hexane : AcOEt = 1 : 1);
NMR : δ 7.75 (2H, m), 7.60 (1H, d, J=2.4Hz), 7.55 (1H, m), 7.45 (2H, m), 7.36 (2H, d, J=8.0Hz), 7.13 (2H, d, J=8.0Hz), 7.03 (1H, brs), 6.96 (1H, dd, J=2.4, 8.8Hz), 6.68 (1H, d, J=8.8Hz), 4.86 (2H, s), 4.73 (2H, d, J=5.8Hz), 1.74 (1H, t, J=5.8Hz).

Example 47

4-[N-[2-(4-chlorophenylsulfonylemino)-5-chlorophenyl]aminosulfonyl]benzoic acid

[0544]



[0545] By using 2-nitro-4-chloroaniline, the title compound having the following physical data was obtained by the same procedure as Reference Example 2→Reference Exemple 12→Reference Example 2→Example 2.

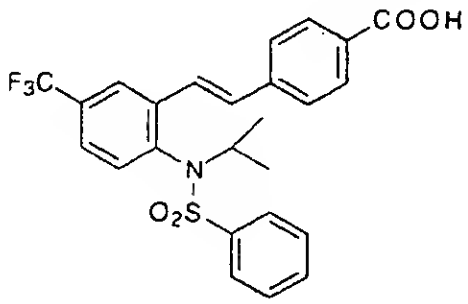
TLC : Rf 0.22 ($CHCl_3$: MeOH : H_2O = 8 : 2 : 0.2);
NMR (DMSO-d_6) : δ 9.68 (1H, br), 8.11 (2H, d, J=8.4Hz), 7.84 (2H, d, J=8.4Hz), 7.69 (2H, d, J=8.8Hz), 7.62 (2H,

d, J=8.8Hz), 7.12 (1H, dd, J=2.4 and 8.4Hz), 7.02 (1H, d, J=2.4Hz), 6.97 (1H, d, J=8.4Hz).

Example 48

4-[2-[2-(N-isopropyl-phenylsulfonylamino)-5-trifluoromethylphenyl]-(E)-vinyl]benzoic acid

[0546]



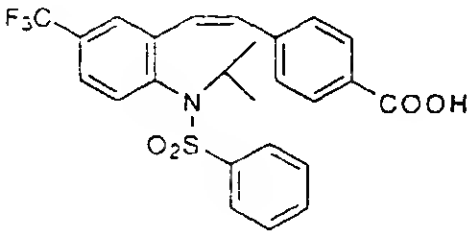
[0547] By using methyl 4-[2-(2-t-butoxycarbonylamino-5-trifluoromethylphenyl)-(E)-vinyl]benzoate, the title compound having the following physical data was obtained by the same procedure as Reference Example 23→Reference Example 2→Example 17→Example 2.

TLC : Rf 0.45 ($CHCl_3$: MeOH = 9 : 1);
NMR : δ 8.2-8.0 (3H, m), 7.9-7.7 (2H, m), 7.6-7.4 (7H, m), 7.2-7.0 (2H, m), 4.8-4.6 (1H, m), 1.08 (3H, d, J=5.0Hz), 1.05 (3H, d, J=5.0Hz).

Example 48(1)

4-[2-[2-(N-isopropyl-phenylsulfonylamino)-5-trifluoromethylphenyl]-(Z)-vinyl]benzoic acid

[0548]



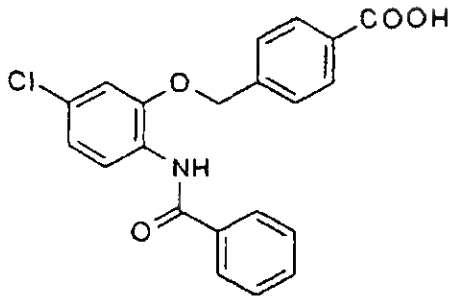
[0549] By using methyl 4-[2-(2-t-butoxycarbonylamino-5-trifluoromethylphenyl)-(Z)-vinyl]benzoate, the title compound having the following physical data was obtained by the same procedure as Reference Example 23→Reference Example 2→Example 17→Example 2.

TLC : Rf 0.51 ($CHCl_3$: MeOH = 9 : 1);
NMR : δ 7.97 (2H, d, J=8.4Hz), 7.9-7.7 (2H, m), 7.7-7.4 (5H, m), 7.31 (2H, d, J=8.4Hz), 7.1-6.9 (2H, m), 6.77 (1H, d, J=12.4Hz), 4.7-4.5 (1H, m), 1.19 (3H, d, J=6.6Hz), 1.04 (3H, d, J=6.6Hz).

Example 49

4-(2-benzoylamino-5-chlorophenoxymethyl)benzoic acid

[0550]



[0551] By using 2-nitro-5-chlorophenol, the title compound having the following physical data was obtained by the same procedure as Reference Example 6→Reference Exemple 12→Example 11→ Example 2.

TLC : Rf 0.51 ($CHCl_3$: MeOH : AcOH= 100 : 5 : 1);
NMR (DMSO-d_6) : δ 12.92 (1H, brs), 9.64 (1H, s), 7.94 (4H, m), 7.75 (1H, d, J=8.6Hz), 7.47-7.68 (5H, m), 7.23 (1H, d, J=2.2Hz), 7.05 (1H, dd, J=2.2, 8.6Hz), 5.32 (2H, s).

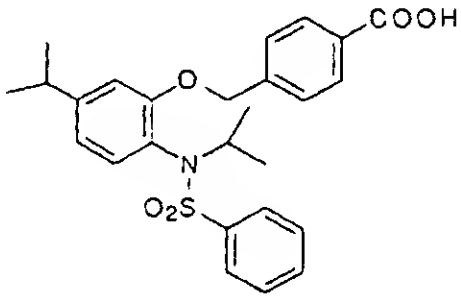
Example 50-50(2)

[0552] By using 4-(2-phenylsulfonylamino-5-isopropylphenoxymethyl)benzoic acid (prepared in Example 40.) or 4-(2-phenylsulfonylamino-5-ethylphenoxymethyl)benzoic acid (prepared in Example 41.), the title compounds having the following physical data were obtained by the same procedure as Reference Example 1→Example 17→Example 2.

Example 50

4-[2-(N-isopropyl-phenylsulfonylamino)-5-isopropylphenoxymethyl]benzoic acid

[0553]



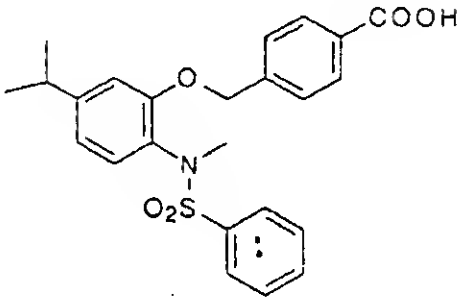
TLC : Rf 0.13 ($CHCl_3$: MeOH = 19 : 1);
NMR (DMSO-d_6) : δ 7.85 (2H, d, J=8Hz), 7.79-7.52(5H, m), 7.40 (2H, d, J=8Hz), 7.01 (1H, d, J=8Hz), 6.73 (1H, d, J=2Hz), 6.65 (1H, dd, J=8 and 2Hz), 4.83 (2H, brs), 4.47 (1H, m), 2.80 (1H, m), 1.1 4 (6H, d, J=7Hz), 0.95 (6H, d,

J=7Hz).

Example 50(1)

4-[2-(N-methyl-phenylsulfonylamino)-5-isopropylphenoxymethyl]benzoic acid

[0554]

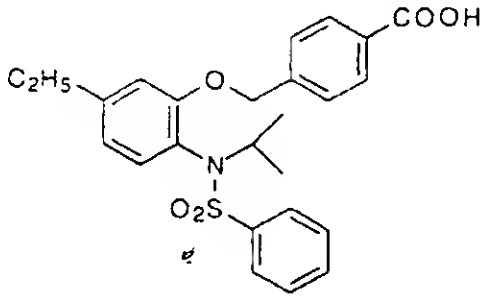


TLC : Rf 0.13 ($CHCl_3$: MeOH = 19 : 1);
NMR ($DMSO-d_6$) : δ 7.85 (2H, d, J=8Hz), 7.76-7.53 (5H, m), 7.39 (2H, d, J=8Hz), 6.98 (1H, d, J=8Hz), 6.77 (1H, d, J=2Hz), 6.70 (1H, dd, J=8 and 2Hz), 4.78 (2H, brs), 3.33 (3H, s), 2.82 (1H, m), 1.15 (6H, d, J=7Hz).

Example 50(2)

4-[2-(N-isopropyl-phenylsulfonylamino)-5-ethylphenoxymethyl]benzoic acid

[0555]

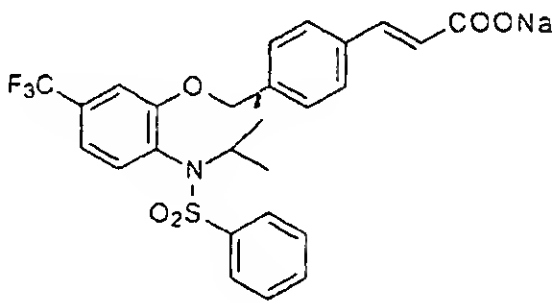


TLC : Rf 0.40 (AcOEt : hexane : AcOH= 5 . 14 . 1);
NMR : δ 7.97 (2H, d, J=8.0Hz), 7.82-7.70 (2H, m), 7.62-7.32 (5H, m), 7.05 (1H, d, J=8.0Hz), 6.60 (1H, dd, J=8, 1.5Hz), 6.53 (1H, d, J=1.5Hz), 4.86 (2H, brs), 4.36 (1H, qn, J=6.0Hz), 2.55 (2H, q, J=7.5Hz), 1.18 (3H, t, J=7.5Hz), 1.02 (6H, brd, J=6.0Hz).

Example 51

4-[2-(N-isopropyl-phenylsulfonylamino)-5-trifluoromethylphenoxymethyl]cinnamic acid · sodium salt

[0556]



[0557] To a solution of 4-[2-(N-isopropyl-phenylsulfonylamino)-5-trifluoromethylphenoxymethyl]cinnamic acid (425 mg; prepared in Example 18(40).) in MeOH (5 ml), 2N NaOH (0.41 ml) wes added. The mixture was stirred at room temperature. The mixture was distilled off azeotropically with benzene three times to give the title compound (430 mg) having the following physical data.

TLC . Rf 0.19 (hexane : AcOEt = 1 : 1);
NMR : δ 7.60 (2H, d, J=7Hz), 7.40-6.97 (11H, m), 6.47 (1H, d, J=16Hz), 4.62 (2H, bs), 4.20-4.08 (1H, m), 0.77 (6H, d, J=5Hz).

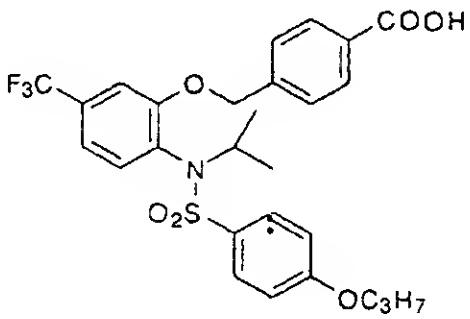
Example 52(1)-52(5)

[0558] By using methyl 4-(2-amino-5-trifluoromethylphenoxymethyl)benzoate (prepared in Reference Example 17.) and the corresponding benzenesulfonylchloride derivatives, the title compounds having the following physical data were obtained by the same procedure as Example 4→Example 19 (isopropanol was used instead of cyclopentylmethanol.)→Example 2.

Example 52(1)

4-[2-(N-isopropyl-4-propoxyphenylsulfonylamino)-5-trifluoromethylphenoxymethyl]benzoic acid

[0559]

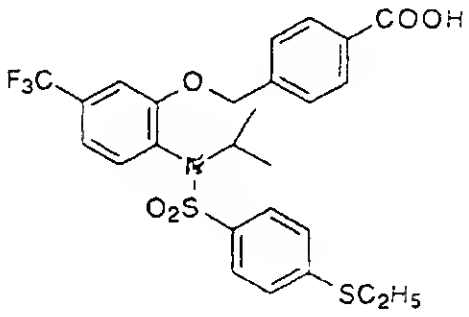


TLC : Rf 0.55 ($CHCl_3$: MeOH = 9 : 1);
NMR : δ 8.16 (2H, d, J=8.8Hz), 7.71 (2H, d, J=8.8Hz), 7.54 (2H, d, J=8.8HZ), 7.30-7.22 (3H, m), 6.80 (2H, d, J=8.8Hz), 5.14 (2H, s), 4.44-4.24 (1H, m), 3.92 (2H, t, J=6.6Hz), 1.91-1.72 (2H, m), 1.14-0.98 (9H, m).

Example 52(2)

4-[2-(N-isopropyl-4-ethylthiophenylsulfonylamino)-5-trifluoromethylphenoxymethyl]benzoic acid

[0560]

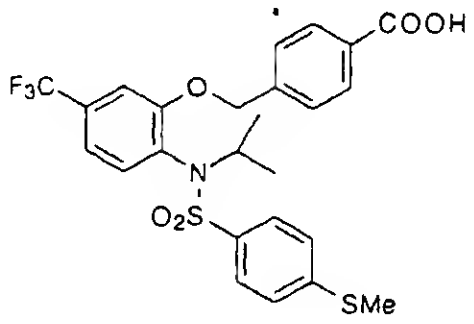


TLC : Rf 0.64 ($CHCl_3$: MeOH = 9 : 1);
NMR : δ 8.17 (2H, d, J=8.4Hz), 7.66 (2H, d, J=8.4Hz), 7.53 (2H, d, J=8.4Hz), .30-7.20 (3H, m), 7.16 (2H, d, J=8.4Hz), 5.12 (2H, s), 4.44-4.22 (1H, m), 2.98 (2H, q, J=7.6Hz), 1.36 (3H, t, J=7.6Hz), 1.09 (3H, d, J=6.6Hz), 1.05 (3H, d, J=6 6Hz).

Example 52(3)

4-[2-(N-isopropyl-4-methylthiophenylsulfonylamino)-5-trifluoromethylphenoxymethyl]benzoic acid

[0561]

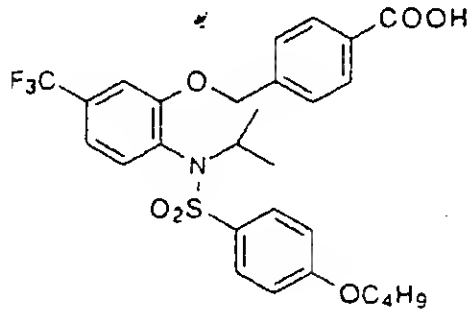


TLC : Rf 0.56 ($CHCl_3$: MeOH = 9 : 1);
NMR : δ 8.16 (2H, d, J=8.4Hz), 7.67 (2H, d, J=8.4Hz), 7.52 (2H, d, J=8.4Hz), 7.30-7.20 (3H, m), 7.12 (2H, d, J=8.4Hz), 5.12 (2H, s), 4.46-4.24 (1H, m), 2.48 (3H, s), 1.09 (3H, d, J=7.0Hz), 1.05 (3H, d, J=7.0Hz).

Example 52(4)

4-[2-(N-isopropyl-4-butoxyphenylsulfonylamino)-5-trifluoromethylphenoxymethyl]benzoic acid

[0562]

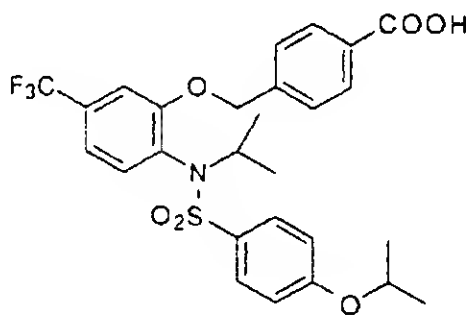


TLC : Rf 0.51 ($CHCl_3$: MeOH = 9 : 1);
NMR : δ 8.16 (2H, d, J=8.4Hz), 7.71 (2H, d, J=8.8Hz), 7.54 (2H, d, J=8.4Hz), 7.30-7.22 (3H, m), 6.79 (2H, d, J=8.8Hz), 5.14 (2H, s), 4.42-4.27 (1H, m), 3.96 (2H, t, J=6.2Hz), 1.87-1.70 (2H, m), 1.60-1.40 (2H, m), 1.14-0.92 (9H, m)

Example 52(5)

4-[2-(N-isopropyl-4-isopropoxyphenylsulfonylamino)-5-trifluoromethylphenoxymethyl]benzoic acid

[0563]



TLC : Rf 0.68 ($CHCl_3$: MeOH = 9 : 1);
NMR : δ 8.17 (2H, d, J=8.0Hz), 7.71 (2H, d, J=8.8Hz), 7.56 (2H, d, J=8.0Hz), 7.30-7.22 (3H, m), 6.78 (2H, d, J=8.8Hz), 5.15 (2H, s), 4.62-4.50 (1H, m), 4.40-4.23 (1H, m), 1.35 (6H, d, J=5.8Hz), 1.08 (3H, d, J=7.4Hz), 1.04 (3H, d, J=7.4Hz).

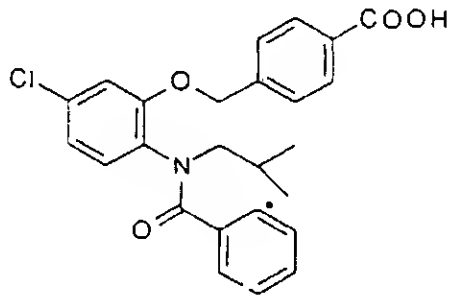
Example 53(1)-53(3)

[0564] By using methyl 4-(2-amino-5-chlorophenoxymethyl)benzoate (prepared in Reference Example 7.) or methyl 4-(2-amino-5-trifluoromethylphenoxymethyl)benzoate (prepared in Reference Example 17.), the title compounds having the following physical data were obtained by the same procedure as Example 27 (the corresponding aldehyde was used.)→Example 11→Example 2.

Example 53(1)

4-[2-(N-isobutyl-benzoylamino)-5-chlorophenoxymethyl]benzoic acid

[0565]

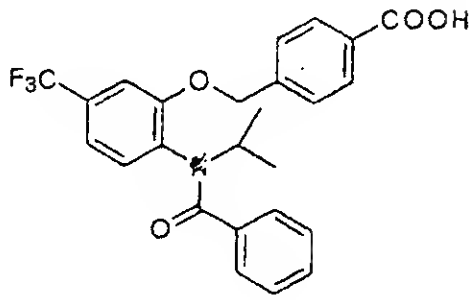


TLC : Rf 0.53 ($CHCl_3$: MeOH = 5 : 1);
NMR($CDCl_3$+1drop of CD_3OD) : δ 8.08 (2H, d, J=8Hz), 7.44-7.04 (8H, m), 6.94-6.80 (1H, m), 6.73 (1H, s), 5.03 (1H, d, J=13Hz), 4.82 (1H, d, J=13Hz), 3.91 (1H, dd, J=15, 7Hz), 3.49 (1H, dd, J=15, 7Hz), 2.10-1.60 (1H, m), 0.98 (6H, d, J=7Hz).

Example 53(2)

4-[2-(N-isopropyl-benzoylamino)-5-trifluoromethylphenoxymethyl]benzoic acid

[0566]

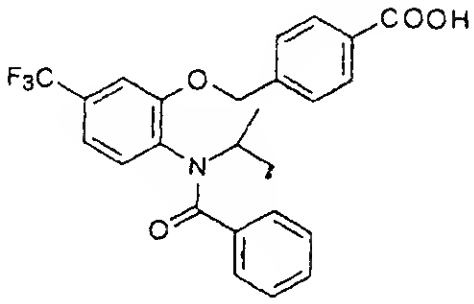


TLC : Rf 0.49 ($CHCl_3$: MeOH = 9 : 1);
NMR : δ 8.18 (2H, d, J=8.4Hz), 7.52-7.35 (3H, m), 7.30-7.03 (6H, m), 7.02-6.92 (1H, m), 5.20-4.90 (2H, m), 4.90-4.70 (1H, m), 1.50-1.00 (6H, m).

Example 53(3)

4-[2-(N-isopropyl-2-furoylamino)-5-trifluoromethylphenoxymethyl]benzoic acid

[0567]

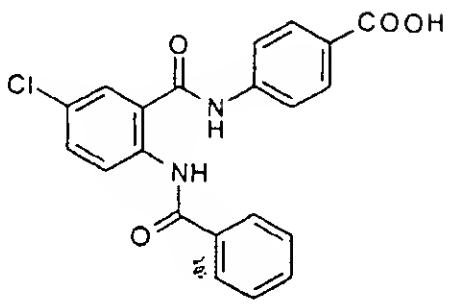


TLC : Rf 0.43 ($CHCl_3$: MeOH = 9 : 1);
NMR : δ 8.09 (2H, d, J=7.8Hz), 7.43-7.22 (5H, m), 7.15 (1H, s), 6.25-6.20 (1H, m), 6.16-6.08 (1H, br), 5.20-4.84 (3H, m), 1.40-1.00 (6H, m).

Example 54

4-(2-benzoylamino-5-chlorobenzoylamino)benzoic acid

[0568]



[0569] By using 2-nitro-5-chlorobenzoic acid chloride (prepared in Reference Example 13.), the title compound having the following physical data was obtained by the same procedure as Example 11→Reference Example 10→Example 11→Example 2.

TLC : Rf 0.52 (AcOEt : hexane : AcOH= 7 : 12 : 1);
NMR (DMSO-d_6) : δ 12.77 (1H, brs), 11.33 (1H, s), 10.85 (1H, s), 8.36 (1H, d, J=9.0Hz), 8.02-7.78 (7H, m), 7.69 (1H, dd, J=9.0, 2.5Hz), 7.64-7.48 (3H, m).

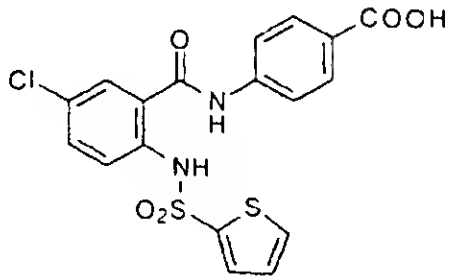
Example 55(1)-55(2)

[0570] By using 2-nitro-5-chlorobenzoic acid chloride (prepared in Reference Example 13.), the title compounds having the following physical data were obtained by the same procedure as Examples 11→Reference Example 10→Reference Example 2→Example 2.

Example 55(1)

4-[2-(2-thienylsulfonylamino)-5-chlorobenzoylamino]benzoic acid

[0571]



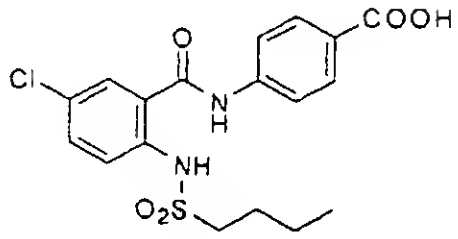
TLC : Rf 0.18 ($CHCl_3$: MeOH = 9 : 1)
NMR (DMSO-d_6) : δ 12.73 (1H, br), 10.68 (1H, brs), 10.48 (1H, brs), 7.93 (2H, d, J=8.8Hz), 7.87 (1H, dd, J=1.2 and 3.6Hz), 7.81 (1H, d, J=2.2Hz), 7.76 (2H, d, J=8.8Hz), 7.61-7.53 (2H, m), 7.41 (1H, d, J=8.8Hz), 7.05 (1H, dd, J=3.8

and 4.0Hz).

Example 55(2)

4-(2-butylsulfonylamino-5-chlorobenzoylamino)benzoic acid

[0572]

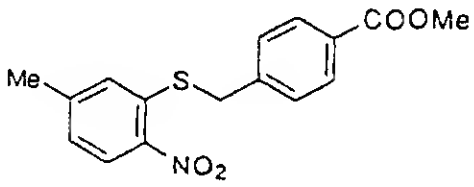


TLC : Rf 0.26 ($CHCl_3$: MeOH = 9 : 1);
NMR (DMSO-d_6) : δ 12.77 (1H, brs), 10.80 (1H, brs), 9.94 (1H, s), 7.93 (2H, d, J=8.8Hz), 7.88 (1H, d, J=2.2Hz), 7.82 (2H, d, J=8.8Hz), 7.61 (1H, dd, J=2.2 and 8.8Hz), 7.54 (1H, d, J=8.8Hz), 3.18 (2H, t-like), 1.66-1.51 (2H, m), 1.37-1.19 (2H, m), 0.74 (3H, t, J=7.2Hz).

Reference Example 51

Methyl 4-(2-nitro-5-methylphenylthiomethyl)benzoate

[0573]



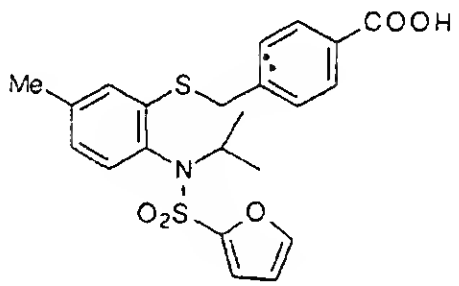
[0574] To a solution of methyl 4-acetylthiomethylbenzoate (794 mg) in MeOH (5.0 ml), sodium methoxide (191 mg) and 3-fluoro-4-nitrotoluene (500 mg) were added suceedingly in a stream of argon at 0°C. The mixture was warmed slowly to become at room temperature. The mixture was stirred for 4 hours. To the reaction mixture, a saturated aqueous ammonium chloride was added. The mixture was extracted with ethyl acetate, washed, dried over and concentrated under the reduced pressure. The residue was recrystrallized from ethanol to give the title compound (646 mg) having the following physical data.

TLC : Rf 0.49 (hexane : CH_2Cl_2 : AcOEt = 8 : 4 : 1).

Example 56

4-[2-(N-isopropyl-2-furanylsulfonylamino)-5-methylphenylthiomethyl]benzoic acid

[0575]



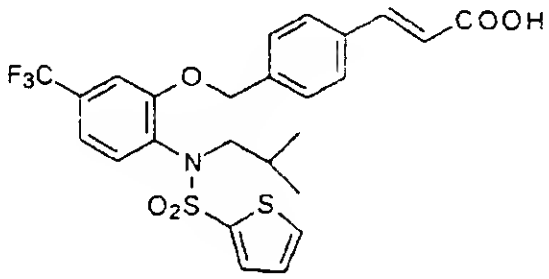
[0576] By using methyl 4-(2-nitro-5-methylphenylthiomethyl)benzoate (prepared in Reference Example 51.), the title compound having the following physical data was obtained by the same procedure as Reference Example 11→Reference Example 2→Example 17→Example 2.

TLC : Rf 0.45 ($CHCl_3$: MeOH : AcOH= 100 : 5 : 1);
NMR : δ 8.04 (2H, d, J=8.4Hz), 7.58 (1H, dd, J=0.8, 1.8Hz), 7.48 (2H, d, J=8.4Hz), 7.08 (1H, m), 6.91-6.98 (2H, m), 6.84 (1H, d, J=8.0Hz), 6.50 (1H, dd, J=2.0, 3.8Hz), 4.47 (1H, sept, J=6.8Hz), 4.19 (2H, s), 2.28 (3H, s), 1.16 (3H, d, J=6.8Hz), 1.06 (3H, d, J=6.8Hz).

Example 57

4-[2-(N-isobutyl-2-thienylsulfonylamino)-5-trifluoromethylphenoxymethyl]cinnamic acid

[0577]



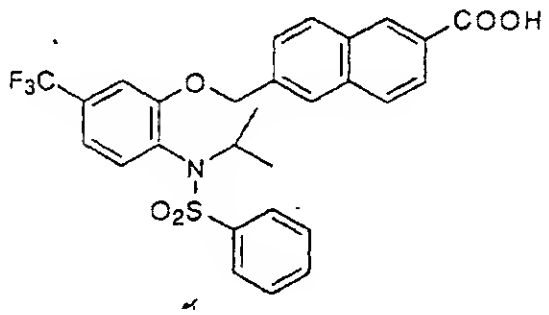
[0578] By using 2-nitro-5-trifluoromethylphenol, the title compound having the following physical data was obtained by the same procedure as Reference Example 18 (b)→Reference Example 12→Reference Example 2→Example 17→Example 2.

TLC : Rf 0.51 ($CHCl_3$: MeOH : AcOH= 100 : 5 : 1);
NMR : δ 7.80 (1H, d, J=16.2Hz), 7.57 (2H, d, J=8.0Hz), 7.22-7.46 (6H, m), 7.16 (1H, m), 6.93 (1H, dd, J=4.0, 5.2Hz), 6.49 (1H, d, J=16.2Hz), 4.94 (2H, brs), 3.45 (2H, d, J=7.2Hz), 1.62 (1H, m), 0.91 (6H, d, J=6.6Hz).

Example 58

6-[2-(N-isopropyl-phenylsulfonylamino)-5-trifluoromethylphenoxymethyl]-2-naphthalic acid

[0579]



[0580] By using 2-(N-isopropyl-phenylsulfonylamino)-5-trifluoromethylphenol (prepared in Reference Example 24.) and ethyl 6-hydroxymethyl-2-naphthate, the title compound having the following physical data was obtained by the same procedure as Reference Example 18 (b)→Example 2.

TLC : Rf 0.55 ($CHCl_3$: MeOH : AcOH = 100 : 5 : 1);
NMR : δ 8.74 (1H, s), 8.17 (1H, dd, J=1.8, 8.8Hz), 8.03 (1H, d, J=8.4Hz), 8.03 (1H, brs), 7.95 (1H, d, J=8.8Hz), 7.79-7.87 (2H, m), 7.61 (1H, dd, J=1.4, 8.4Hz), 7.43 (1H, m), 7.32 (3H, m), 7.26 (2H, m), 5.26 (2H, s), 4.39 (1H, m), 1.08 (3H, d, J=6.6Hz), 1.06 (3H, d, J=6.6Hz).

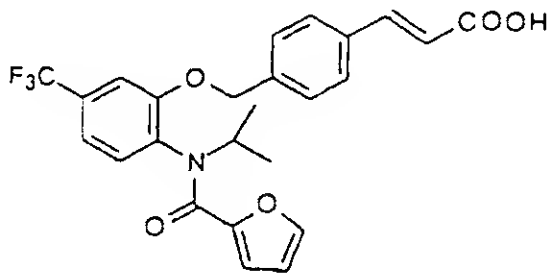
Example 59(1)-59(3)

[0581] By using 2-nitro-5-trifluoromethylphenol, the title compounds having the following physical data were obtained by the same procedure es Reference Example 18 (b)→Reference Example 12→Example 27→Example 11→Exemple 2.

Example 59(1)

4-[2-(N-isopropyl-2-furoylamino)-5-trifluoromethylphenoxymethyl]cinnamic acid

[0582]



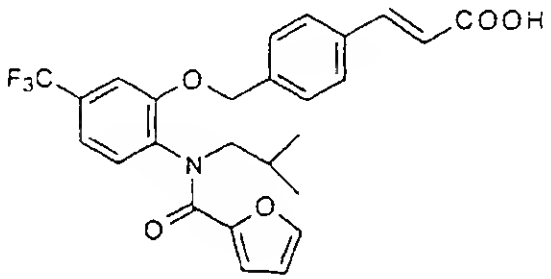
TLC : Rf 0.44 ($CHCl_3$: MeOH = 9 : 1);

NMR : δ 7.76 (1H, d, J=16.2Hz), 7.52 (2H, d, J=8.4Hz), 7.38 (1H, d, J=8.4Hz), 7.32 (1H, d, J=8.4Hz), 7.28-7.20 (3H, m), 7.17 (1H, s), 6.45 (1H, d, J=16.2Hz), 6.24-6.19 (1H, m), 6.11-6.00 (1H, br), 5.20-4.80 (3H, m), 1.40-1.00 (6H, m).

Example 59(2)

4-[2-(N-isobutyl-2-furoylamino)-5-trifluoromethylphenoxymethyl]cinnamic acid

[0583]

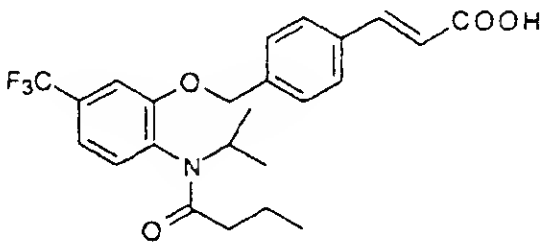


TLC : Rf 0.49 ($CHCl_3$: MeOH = 9 : 1);
NMR : δ 7.76 (1H, d, J=15.9Hz), 7.52 (2H, d, J=8.4Hz), 7.39 (1H, d, J=8.1Hz), 7.33-7.15 (5H, m), 6.45 (1H, d, J=15.9Hz), 6.28-6.10 (2H, m), 5.20-4.90 (2H, m), 4.00-3.80 (1H, br), 3.60-3.30 (1H, br), 2.00-1.80 (1H, m), 0.95 (6H, d, J=6.6Hz).

Example 59(3)

4-[2-(N-isopropyl-butyrylamino)-5-trifluoromethylphenoxymethyl]cinnamic acid

[0584]



TLC : Rf 0.42 ($CHCl_3$: MeOH = 9 : 1);
NMR . δ 7.78 (1H, d, J=15.9Hz), 7.58 (2H, d, J=8.1Hz), 7.42 (2H, d, J=8.1Hz), 7.35-7.20 (3H, m), 6.48 (1H, d, J=15.9Hz), 5.20-4.93 (3H, m), 1.90 (2H, dt, J=2.7, 7.5Hz), 1.64-1.50 (2H, m), 1.17 (3H, d, J=6.6Hz), 0.94 (3H, d, J=6.6Hz),

0.79 (3H, t, J=7.2Hz).

Example 60(1)-60(2)

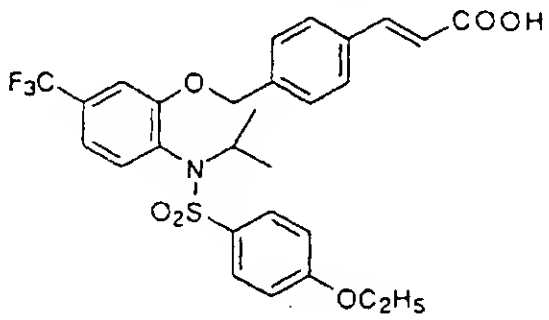
[0585] By using 2-nitro-5-trifluoromethylphenol, the title compounds having the following physical data were obtained

by the same procedure as Reference Example 18 (b)→Reference Example 12→Referenc Example 2→Example 19→Example 2.

Example 60(1)

4-[2-(N-isopropyl-4-ethoxyphenylsulfonylamino)-5-trifluoromethylphenoxymethyl]cinnamic acid

[0586]

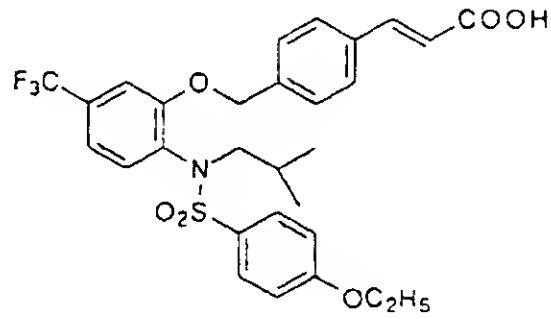


TLC : Rf 0.51 ($CHCl_3$: MeOH = 9 : 1);
NMR : δ 7.82 (1H, d, J=16.0Hz), 7.72 (2H, d, J=8.8Hz), 7.61 (2H, d, J=8.6Hz), 7.48 (2H, d, J=8.6Hz), 7.28-7.22 (3H, m), 6.77 (2H, d, J=8.8Hz), 6.50 (1H, d, J=16.0Hz), 5.10 (2H, s), 4.40-4.20 (1H, m), 4.01 (2H, q, J=6.8Hz), 1.43 (3H, t, J=6.8Hz), 1.07 (3H, d, J=6.6Hz), 1.03 (3H, d, J=6.6Hz).

Example 60(2)

4-[2-(N-isobutyl-4-ethoxyphenylsulfonylamino)-5-trifluoromethylphenoxymethyl]cinnamic acid

[0587]

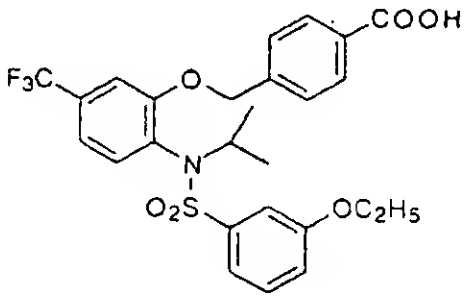


TLC : Rf 0.57 ($CHCl_3$: MeOH = 9 : 1);
NMR : δ 7.81(1H, d, J=15.6Hz), 7.60-7.47 (3H, m), 7.44 (1H, d, J=8.2Hz), 7.30-7.10 (5H, m), 6.73(2H, d, J=8.8Hz), 6.50 (1H, d, J=15.6Hz), 5.00-4.80 (2H, br), 3.95 (2H, q, J=7.0Hz), 3.39 (2H, d, J=6.8Hz), 1.70-1.50 (1H, m), 1.41 (3H, t, J=6.8Hz), 0.88 (6H, d, J=6.6Hz).

Example 61

4-[2-(N-isopropyl-3-ethoxyphenylsulfonylamino)-5-trifluoromethylphenoxymethyl]benzoic acid

[0588]



[0589] By using methyl 4-(2-amino-5-trifluoromethylphenoxymethyl)benzoate (prepared in Reference Example 17.), the title compound having the following physical data was obtained by the same procedure as Exemple 4→Exemple 19→Example 2.

TLC : Rf 0.63 ($CHCl_3$: MeOH = 9 : 1);
NMR : δ 8.15 (2H, d, J=8.4Hz), 7.53 (2H, d, J=8.4Hz), 7.40-7.20 (6H, m), 7.02 (1H, ddd, J=1.2, 2.4, 8.0Hz), 5.13 (2H, s), 4.52-4.36 (1H, m), 3.98 (2H, q, J=6.8Hz), 1.40 (3H, t, J=6.8Hz), 1.08 (3H, d, J=6.6Hz), 1.06 (3H, d, J=6.6Hz).

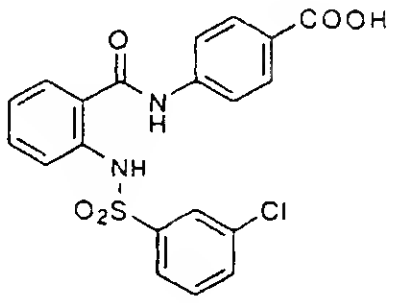
Example 62(1)-62(2)

[0590] By using 2-nitrobenzoic acid chloride, the title compounds having the following physical data were obtained by the same procedure es Example 11→Reference Example 20→Reference Example 2→Example 2.

Example 62(1)

4-[2-(3-chlorophenylsulfonylamino)benzoylamino]benzoic acid

[0591]



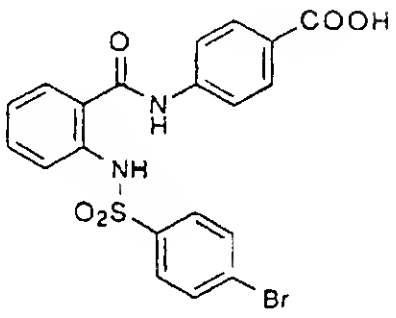
TLC : Rf 0.38 ($CHCl_3$: MeOH = 9 : 1);
NMR (DMSO-d_6) : δ 10.59 (1H, s), 10.44 (1H, s), 7.95 (2H, d, J=8.4Hz), 7.86-7.60 (6H, m), 7.58-7.45 (2H, m), 7.38-

7.25 (2H, m).

Example 62(2)

4-[2-(4-bromophenylsulfonylamino)benzoylamino]benzoic acid

[0592]



TLC : Rf 0.39 ($CHCl_3$: MeOH = 9 : 1);
NMR (DMSO-d_6) : δ 10.55 (1H, s), 10.38 (1H, s), 7.96 (2H, d, J=8.8Hz), 7.90-7.45 (8H, m), 7.44-7.25 (2H, m).

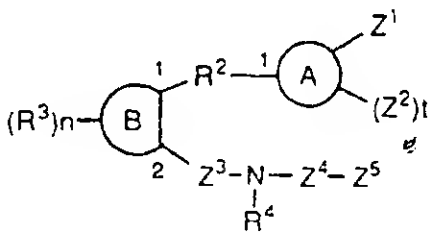
Formulation example 1

[0593] The following compounds were admixed in conventional method and punched out to obtain 100 tablets each containing 5 mg of active ingredient.

• 4-(2-phenylsulfonylamino-5-chlorobenzoylamino)benzoic acid (prepared in Example 2.)	500 mg
• Cellulose calcium glycolate (disintegrating agent)	200 mg
• Magnesium stearate (lubricating agent)	100 mg
• Micro crystalline cellulose	9.2 g

Claims

1. A sulfonamide or carboamide derivative of the formula (I)



(I)

(wherein

and

each, independently, is C5-15 carbocyclic ring or 5-7 membered heterocyclic ring containing one or two oxygen, sulfur or nitrogen atom(s),

Z^1 is

-COR^1,
-C1-4 alkylene-COR^1,
-CH=CH-COR^1,
-C≡COR^1, or
-O-C1-3 alkylene-COR^1,
(wherein, R^1 is hydroxy, C1-4 alkoxy or formula

$$NR^6R^7$$

(wharain, R^6 and R^7 each, independantly, is H or C1-4 alkyl.).), or
-C1-5 alkylene-OH,

Z^2 is H, C1-4 alkyl, C1-4 alkoxy, nitro, halogen, trifluoromethyl, trifluoromethoxy, hydroxy or COR^1 (wherein R^1 is as defined herainbefora.),
Z^3 is single bond or C1-4 alkylene,
Z^4 is SO_2 or CO,
Z^5 is

(1) C1-8 alkyl, C2-8 alkenyl, or C2-8 alkynyl,
(2) phenyl, C3-7 cycloalkyl, or 5-7 membered heterocyclic ring containing one or two oxygen, sulfur or nitrogan atom(s), or
(3) C1-4 alkyl, C2-4 alkenyl or C2-4 alkynyl substituted by phenyl or C3-7 cycloalkyl

(phenyl, C3-7 cycloalkyl and 5-7 membered heterocyclic ring containing one or two oxygen, sulfur or nitrogen atom(s) mentioned in the above (2) and (3) may ba substituted by 1-5 of R^5 (wherein R^5 (if two or more R^5, each independently) is H, C1-6 alkyl, C1-6 alkoxy, C1-6 alkylthio, nitro, halogen, tifluoromethyl, trifluoromethoxy or hydroxy.).),
R^2 is

$CONR^8$,
NR^8CO,
$CONR^8$-C1-4 alkylene,
C1-4 alkylena-$CONR^8$,
NR^6CO-C1-4 alkylene,
C1-4 alkylene-NR^8CO,
C1-3 alkylene-$CONR^9$-C1-3 alkylane, or
C1-3 alkylene-NR^8CO-C1-3 alkylene
(wherein each R^8 is H or C1-4 alkyl.),
O, S, NZ^6
(wherein Z^6 is H or C1-4 alkyl.),

Z^7-C1-4 alkylene,
C1-4 alkylene-Z^7, or
C1-3 alkylena-Z^7-C1-3 alkylena
(wherein each Z^7 is O, S or NZ^6 (wherein Z^6 is as defined hereinbefore.).)
CO,
CO-C1-4 alkylene,
C1-4 alkylene-CO,
C1-3 alkylene-CO-C1-3 alkylene,
C2-4 alkylene,
C2-4 alkenylene, or
C2-4 alkynylene,

R^3 is H, C1-6 alkyl, C1-6 alkoxy, C1-6 alkylthio, nitro, halogen, trifluoromethyl, trifluoromethoxy, hydroxy or hydroxymethyl,
R^4 is

(1) H,
(2) C1-8 alkyl, C2-8 alkenyl, or C2-8 alkynyl,
(3) C1-6 alkyl substituted by one or two substituent(s) selected from the group consisting of $COOZ^8$, $CONZ^9Z^{10}$, and OZ^8 (wherein Z^8, Z^9 and Z^{10} each, independently, is H or C1-4 alkyl.) and C1-4 alkoxy-C1-4 alkoxy,
(4) C3-7 cycloalkyl, or
(5) C1-4 alkyl, C2-4 alkenyl or C2-4 alkynyl substituted by phenyl or C3-7 cycloalkyl

(phenyl and C3-7 cycloalkyl mentioned in the above (4) and (5) may be substituted by 1-5 of R^5 (wherein R^5 is as defined hereinbefore.).), and n and t each, independently, is an integer of 1-4,
with the proviso that (1) R^2 and Z^3 should be connected at the 1- or 2- position of

, and (2) when

is a benzene ring and $(Z^2)t$ is other than COR^1, Z^1 should be connected at the 3- or 4-position of the benzene ring.), or a non-toxic salt thereof.

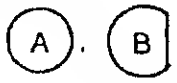
2. A compound according to claim 1, wherein

and

is C5-15 carbocyclic ring and Z^5 is C1-8 alkyl, C2-8 alkenyl, C2-8 alkynyl, or group containing phenyl or C3-7

cycloalkyl.

3. A compound according to claim 1, wherein at least one of



and Z^5 is 5-7 membered heterocyclic ring containing one or two oxygen, sulfur or nitrogen atom(s).

4. A compound according to claim 1 or 3, wherein

and

is C5-15 carbocyclic ring and Z^5 is 5-7 membered heterocyclic ring containing one or two oxygen, sulfur or nitrogen atom(s).

5. A compound according to claim 1 or 3, wherein one of

and

is 5-7 membered heterocyclic ring containing one or two oxygen, sulfur or nitrogen atom(s) and the other is C5-15 carbocyclic ring.

6. A compound according to claim 1, 2 or 3, wherein R^2 is

$CONR^8$,
$CONR^8$-C1-4 alkylene,
C1-4 alkylene-$CONR^6$,
C1-3 alkylene-$CONR^6$-C1-3 alkylene,
NR^8CO,
NR^8CO-C1-4 alkylene,
C1-4 alkylene-NR^8CO or
C1-3 alkylene-NR^8CO-C1-3 alkylene
(wherein each R^8 is H or C1-4 alkyl.).

7. A compound according to claim 1, 2 or 3, wherein R^2 is

O, S, NZ^6
(wherein Z^6 is H or C1-4 alkyl.),
Z^7-C1-4 alkylene,
C1-4 alkylene-Z^7, or
C1-3 alkylene-Z^7-C1-3 alkylene
(wherein each Z^7 is O, S or NZ^6 (wherein Z^6 is as defined hereinbefore.).).

8. A compound according to claim 1, 2 or 3, wherein R^2 is

C2-4 alkylene, C2-4 alkenylene or C2-4 alkynylene.

9. A compound according to claim 1, 2 or 3, wherein R^2 is

CO,
CO-C1-4 alkylene,
C1-4 alkylene-CO or
C1-3 alkylene-CO-C1-3 alkylene.

10. A compound according to claim 1 which is selected from

(1) 4-(2-phenylsulfonylamino-5-chlorobenzoylamino)benzoic acid,
(2) 3-(2-phenylsulfonylaminobenzoylamino)benzoic acid,
(3) 3-(2-phenylsulfonylamino-5-chlorobenzoylamino)benzoic acid,
(4) 4-(2-phenylsulfonylaminobenzoylamino)benzoic acid,
(5) 4-[2-(4-chlorophenyl)sulfonylamino-5-chlorobenzoylamino]benzoic acid,
(6) 4-[2-(4-chlorophenylsulfonylamino)-4-chlorobenzoylamino]benzoic acid,
(7) 4-[2-(4-chlorophenylsulfonylamino)-6-chlorobenzoylamino]benzoic acid,
(8) 4-[2-(4-chlorophenylsulfonylamino)-3-chlorobenzoylamino]benzoic acid,
(9) 4-[2-(2-chlorophenylsulfonylamino)-5-chlorobenzoylamino]benzoic acid,
(10) 4-[2-(3-chlorophenylsulfonylamino)-5-chlorobenzoylamino]benzoic acid,
(11) 4-[2-(4-chlorophenylsulfonylamino)-5-fluorobenzoylamino]benzoic acid,
(12) 4-[2-(4-chlorophenylsulfonylamino)-5-bromobenzoylamino]benzoic acid,
(13) 4-[2-(4-chlorophenylsulfonylamino)-5-methoxybenzoylamino]benzoic acid,
(14) 4-[2-(4-bromophenylsulfonylamino)-5-chlorobenzoylamino]benzoic acid,
(15) 4-[2-(4-methylphenylsulfonylamino)-5-chlorobenzoylamino]benzoic acid,
(16) 4-[2-(4-methoxyphenylsulfonylamino)-5-chlorobenzoylamino]benzoic acid,
(17) 4-[2-(4-nitrophenylsulfonylamino)-5-chlorobenzoylamino]benzoic acid,
(18) 4-[2-(2,4-dichlorophenylsulfonylamino)-5-chlorobenzoylamino]benzoic acid,
(19) 4-[2-(4-n-butylphenylsulfonylamino)-5-chlorobenzoylamino]benzoic acid,
(20) 4-[2-(4-chlorophenylsulfonylamino)benzoylamino]benzoic acid,
(21) 4-(2-phenylsulfonylamino-5-fluorobenzoylamino)benzoic acid,
(22) 4-(2-phenylsulfonylamino-4-fluorobenzoylamino)benzoic acid,
(23) 4-[2-(4-chlorophenylsulfonylamino)-4-fluorobenzoylamino]benzoic acid,
(24) 4-[2-(4-fluorophenylsulfonylamino)-5-chlorobenzoylamino]benzoic acid,
(25) 4-[2-(4-trifluoromethylphenylsulfonylamino)-5-chlorobenzoylamino]benzoic acid,
(26) 4-(2-phenylsulfonylamino-5-chlorobenzoylaminomethyl)benzoic acid,
(27) 4-[2-(2-phenylvinyl)sulfonylamino-5-chlorobenzoylamino]benzoic acid,
(28) 4-[2-(2-phenylethyl)sulfonylamino-5-chlorobenzoylamino]benzoic acid,
(29) 4-[2-(4-chlorophenylsulfonylamino)-5-nitrobenzoylamino]benzoic acid,
(30) 4-[2-(4-hydroxyphenylsulfonylamino)-5-chlorobenzoylamino]benzoic acid,
(31) 4-(2-phenylsulfonylamino-5-chlorophenylaminocarbonyl)benzoic acid,
(32) 4-[2-(N-isopropyl-phenylsulfonylamino)-5-trifluoromethylbenzoylamino]benzoic acid,
(33) 4-[N-[2-(4-chlorophenylsulfonylamino)-5-chlorophenyl]aminosulfonyl]benzoic acid,
(34) 4-(2-benzoylamino-5-chlorobenzoylamino)benzoic acid,
(35) 4-(2-butylsulfonylamino-5-chlorobenzoylamino)benzoic acid,
(36) 4-[2-(3-chlorophenylsulfonylamino)benzoylamino]benzoic acid and
(37) 4-[2-(4-bromophenylsulfonylamino)benzoylamino]benzoic acid, and methyl esters thereof.

11. A compound according to claim 1 which is selected from

(1) 4-[2-(4-chlorophenylsulfonylamino)-5-chlorophenoxymethyl]benzoic acid,
(2) 4-(2-phenylsulfonylamino-5-chlorophenoxymethyl)benzoic acid,
(3) 4-(2-phenylsulfonylamino-4-chlorophenoxymethyl)benzoic ecid,
(4) 4-[2-(4-chlorophenylsulfonylamino)-4-chlorophenoxymethyl]benzoic acid,
(5) 4-[2-(4-chlorophenylsulfonylamino)-5-chlorophenylmethoxy]benzoic acid,
(6) 4-(2-phenylsulfonylamino-5-trifluoromethylphenoxymethyl)benzoic ecid,
(7) 4-[2-(N-isopropyl-phenylsulfonylamino)-4-chlorophenoxymethyl]benzoic acid,
(8) 4-[2-(N-carboxymethyl-phenylsulfonylamino)-4-chlorophenoxymethyl]benzoic acid,
(9) 4-[2-[N-(2-hydroxyethyl)-phenylsulfonylamino]-4-chlorophenoxymethyl]benzoic acid,
(10) 4-[2-(N-methyl-phenylsulfonylamino)-4-trifluoromethylphenoxymethyl]benzoic acid,
(11) 4-[2-[N-(2-hydroxyethyl)-phenylsulfonylamino]-4-trifluoromethylphenoxymethyl]benzoic acid,
(12) 4-[2-[N-(2-hydroxyethyl)-phenylsulfonylamino]-5-trifluoromethylphenoxymethyl]benzoic acid,
(13) 4-[2-(N-methyl-phenylsulfonylamino)-5-chlorophenoxymethyl]benzoic ecid,
(14) 4-[2-[N-(2-hydroxyethyl)-phenylsulfonylemino]-5-chlorophenoxymethyl]benzoic acid,
(15) 4-[2-(N-methyl-phenylsulfonylamino)-5-trifluoromethylphenoxymethyl]benzoic acid,
(16) 4-[2-(N-isopropyl-phenylsulfonylamino)-5-trifluoromethylphenoxymethyl]benzoic acid,
(17) 4-[2-(N-isopropyl-phenylsulfonylamino)-5-chlorophenoxymethyl]benzoic ecid,
(18) 4-[2-(N-isopropyl-phenylsullonylamino)-4-trifluoromethylphenoxymethyl]benzoic acid,
(19) 4-[2-[N-(2-methoxyethoxymethyl)-phenylsullonylamino]-4-chlorophenoxymethyl]benzoic acid,
(20) 4-[2-[N-(2-methoxyethyl)-phenylsulfonylamino]-4-chlorophenoxymethyl]benzoic acid,
(21) 4-[2-[N-[2-(2-methoxyethoxy)ethyl]-phenylsulfonylamino]-4-chlorophenoxymethyl]benzoic acid,
(22) 4-[2-(N-ethyl-phenylsulfonylamino)-4-chlorophenoxymethyl]benzoic acid,
(23) 4-(2-(N-propyl-phenylsulfonylamino)-4-chlorophenoxymethyl]benzoic acid,
(24) 4-[2-(N-butyl-phenylsulfonylemino)-4-chlorophenoxymethyl]benzoic ecid,
(25) 4-[2-(N-pentyl-phenylsulfonylamino)-4-chlorophenoxymethyl]benzoic acid,
(26) 4-[2-(N-hexyl-phenylsulfonylamino)-4-chlorophenoxymethyl]benzoic acid,
(27) 4-[2-(N-benzyl-phenylsulfonylamino)-4-chlorophenoxymethyl]benzoic acid,
(28) 4-[2-(N-isopropyl-phenylsulfonylemino)-5-methylphenoxymethyl]benzoic acid,
(29) 4-[2-(N-methyl-phenylsulfonylamino)-5-methylphenoxymethyl]benzoic acid,
(30) 4-[2-[N-(2-hydroxyethyl)-phenylsulfonylamino]-5-methylphenoxymethyl]benzoic acid,
(31) 4-[2-[N-(prop-2-enyl)-phenylsulfonylamino]-4-chlorophenoxymethyl]benzoic acid,
(32) 4-[2-(N-cyclopentyl-phenylsulfonylamino)-4-chlorophenoxymethyl]benzoic acid,
(33) 4-[2-[N-(2-methoxyethyl)-phenylsulfonylamino]-5-trifluoromethylphenoxymethyl]benzoic acid,
(34) 4-[2-(N-ethyl-phenylsulfonylamino)-5-trifluoromethylphenoxymethyl]benzoic acid,
(35) 4-[2-(N-propyl-phenylsulfonylamino)-5-trifluoromethylphenoxymethyl]benzoic acid,
(36) 4-[2-(N-isobutyl-phenylsulfonylamino)-5-trifluoromethylphenoxymethyl]benzoic acid,
(37) 4-[2-(N-cyclopentyl-phenylsulfonylamino)-5-trifluoromethylphenoxymethyl]benzoic acid,
(38) 4-[2-[N-(prop-2-enyl)-phenylsulfonylamino]-5-trifluoromethylphenoxymethyl]benzoic acid,
(39) 4-[2-[N-(2-methylprop-2-enyl)-phenylsulfonylemino]-5-trifluoromethylphenoxymethyl]benzoic ecid,
(40) 4-[2-(N-isopropyl-4-methylphenylsulfonylamino)-5-trifluoromethylphenoxymethyl]benzoic acid,
(41) 4-[2-(N-isopropyl-4-fluorophenylsulfonylamino)-5-trifluoromethylphenoxymethyl]benzoic acid,
(42) 4-[2-(N-isopropyl-4-methoxyphenylsulfonylamino)-5-trifluoromethylphenoxymethyl]benzoic ecid,
(43) 4-[2-(N-isopropyl-phenylsulfonylamino)-5-chlorophenoxy]benzoic acid,
(44) 3-[2-(N-isopropyl-phenylsulfonylamino)-5-chlorophenoxy]cinnamic acid,
(45) trans-4-[2-(N-isopropyl-phenylsulfonylamino)-5-trifluoromethylphenoxymethyl]cyclohexanoic acid,
(46) 4-[2-(N-isopropyl-phenylsulfonylamino)-5-chlorophenoxy]phenylecetic ecid,
(47) 4-[2-(N-isopropyl-phenylsulfonylamino)-5-trifluoromethylphenoxymethyl]cinnamic acid,
(48) 3-[4-[2-(N-isopropyl-phenylsulfonylamino)-5-trifluoromethylphenoxymethyl]phenyl]propionic acid,
(49) 3-[2-(N-isopropyl-phenylsulfonylemino)-5-trifluoromethylphenoxymethyl]phenylacetic acid,
(50) 4-[2-(N-isopropyl-4-ethoxyphenylsulfonylamino)-5-trifluoromethylphenoxymethyl]benzoic ecid,
(51) 4-[2-(N-isobutyl-phenylsulfonylamino)-5-methylphenoxymethyl]benzoic ecid,
(52) 4-[2-(N-isopropyl-phenylsulfonylamino)-5-fluorophenoxymethyl]benzoic acid,
(53) 4-[2-(N-isopropyl-phenylsulfonylamino)-5-methoxyphenoxymethyl]benzoic ecid,
(54) 4-[2-(N-propyl-phenylsullonylamino)-5-methylphenoxymethyl]benzoic acid,
(55) 4-[2-[N-(prop-2-enyl)-phenylsullonylamino]-5-methylphenoxymethyl]benzoic acid,
(56) 4-[2-[N-(2-methylprop-2-enyl)-phenylsulfonylamino]-5-methylphenoxymethyl]benzoic acid,

(57) 4-[2-(N-cyclopropylmethyl-phenylsulfonylamino)-5-methylphenoxymethyl]benzoic acid,
(58) 4-[2-(N-propyl-phenylsulfonylamino)-5-chlorophenoxymethyl]benzoic acid,
(59) 4-[2-(N-isobutyl-phenylsulfonylamino)-5-chlorophenoxymethyl]benzoic acid,
(60) 4-[2-[N-(prop-2-enyl)-phenylsulfonylamino]-5-chlorophenoxymethyl]benzoic acid,
(61) 4-[2-[N-(2-methylprop-2-enyl)-phenylsulfonylamino]-5-chlorophenoxymethyl]benzoic acid,
(62) 4-[2-(N-cyclopropylmethyl-phenylsulfonylamino)-5-chlorophenoxymethyl]benzoic acid,
(63) 4-[2-(N-methoxymethyl-phenylsulfonylamino)-5-trifluoromethylphenoxymethyl]benzoic acid,
(64) 4-[2-(N-isobutyl-phenylsulfonylamino)-4-methylphenoxymethyl]benzoic acid,
(65) 4-[2-(N-isopropyl-phenylsulfonylamino)-4-methylphenoxymethyl]benzoic acid,
(66) 4-[2-[N-(prop-2-enyl)-phenylsulfonylamino]-4-methylphenoxymethyl]benzoic acid,
(67) 4-[2-(N-isopropyl-4-ethoxyphenylsulfonylamino)-5-chlorophenoxymethyl]benzoic acid,
(68) 4-[2-(N-isopropyl-4-ethoxyphenylsulfonylamino)-5-methylphenoxymethyl]benzoic acid,
(69) 4-[2-(N-ethyl-phenylsulfonylamino)-4-methylphenoxymethyl]benzoic acid,
(70) 4-[2-(N-propyl-phenylsulfonylamino)-4-methylphenoxymethyl]benzoic acid,
(71) 4-[2-(N-butyl-phenylsulfonylamino)-4-methylphenoxymethyl]benzoic acid,
(72) 4-[2-[N-(2-methylprop-2-enyl)-phenylsulfonylamino]-4-methylphenoxymethyl]benzoic acid,
(73) 4-[2-(N-cyclopropylmethyl-phenylsulfonylamino)-4-methylphenoxymethyl]benzoic acid,
(74) 4-[2-(N-isopropyl-propylsulfonylamino)-5-methylphenoxymethyl]benzoic acid,
(75) 4-[2-(N-isopropyl-pentylsulfonylamino)-5-methylphenoxymethyl]benzoic acid,
(76) 4-[2-(N-benzyl-methylsulfonylamino)-5-methylphenoxymethyl]benzoic acid,
(77) 4-[2-(N-benzyl-propylsulfonylamino)-5-methylphenoxymethyl]benzoic acid,
(78) 4-[2-(N-isopropyl-cyclopentylsulfonylamino)-5-methylphenoxymethyl]benzoic acid,
(79) 4-[2-(N-isobutyl-ethylsulfonylamino)-4-methylphenoxymethyl]benzoic acid,
(80) 4-[2-(N-isobutyl-propylsulfonylamino)-4-methylphenoxymethyl]benzoic acid,
(81) 4-[2-(N-isobutyl-butylsulfonylamino)-4-methylphenoxymethyl]benzoic acid,
(82) 4-[2-(N-isobutyl-propylsulfonylamino)-5-methylphenoxymethyl]benzoic acid,
(83) 4-[2-[N-(prop-2-enyl)-propylsulfonylamino]-5-methylphenoxymethyl]benzoic acid,
(84) 4-[2-[N-(2-methylprop-2-enyl)-propylsulfonylamino]-5-methylphenoxymethyl]benzoic acid,
(85) 4-[2-(N-isobutyl-phenylsulfonylamino)-4-chlorophenoxymethyl]benzoic acid,
(86) 4-[2-(N-propyl-propylsulfonylamino)-5-methylphenoxymethyl]benzoic acid,
(87) 4-[2-(N-isobutyl-hexylsulfonylamino)-4-methylphenoxymethyl]benzoic acid,
(88) 4-[2-(N-isobutyl-pentylsulfonylamino)-4-methylphenoxymethyl]benzoic acid,
(89) 4-[2-[N-(prop-2-enyl)-propylsulfonylamino]-5-trifluoromethylphenoxymethyl]benzoic acid,
(90) 4-[2-[N-(2-methylprop-2-enyl)-propylsulfonylamino]-5-trifluoromethylphenoxymethyl]benzoic acid,
(91) 4-[2-(N-propyl-propylsulfonylamino)-5-trifluoromethylphenoxymethyl]benzoic acid,
(92) 4-[2-(N-isobutyl-propylsulfonylamino)-5-trifluoromethylphenoxymethyl]benzoic acid,
(93) 4-[2-(N-propyl-phenylsulfonylamino)-5-methylphenoxymethyl]cinnamic acid,
(94) 4-[2-(N-isobutyl-phenylsulfonylamino)-5-methylphenoxymethyl]cinnamic acid,
(95) 4-[2-(N-isobutyl-propylsulfonylamino)-5-trifluoromethylphenoxymethyl]cinnamic acid,
(96) 4-[2-(N-methyl-phenysulphonylamino)-5-trifluoromethylphenoxymethyl]cinnamic acid,
(97) 4-[2-(N-propyl-phenylsulfonylamino)-5-trifluoromethylphenoxymethyl]cinnamic acid,
(98) 4-[2-(N-isobutyl-phenylsulfonylamino)-5-trifluoromethylphenoxymethyl]cinnamic acid,
(99) 4-[2-(N-isopropyl-propylsulfonylamino)-5-methylphenoxymethyl]cinnamic acid,
(100) 4-[2-(N-ethyl-phenylsulfonylamino)-5-trifluoromethylphenoxymethyl]cinnamic acid,
(101) 4-[2-(N-cyclopropylmethyl-phenylsulfonylamino)-5-trifluoromethylphenoxymethyl]cinnamic acid,
(102) 4-[2-(N-isopropyl-methylsulfonylamino)-5-trifluoromethylphenoxymethyl]cinnamic acid,
(103) 4-[2-(N-benzyl-propylsulfonylamino)-5-trifluoromethylphenoxy-ethyl]cinnamic acid,
(104) 4-[2-(N-propyl-phenylsulfonylamino)-4-methylphenoxymethyl]cinnamic acid,
(105) 4-[2-[N-(prop-2-enyl)-phenylsulfonylamino]-5-trifluoromethylphenoxymethyl]cinnamic acid,
(106) 4-[2-[N-(2-methylprop-2-enyl)-phenylsulfonylamino]-5-trifluoromethylphenoxymethyl]cinnamic acid,
(107) 4-[2-(N-isobutyl-phenylsulfonylamino)-4-methylphenoxymethyl]cinnamic acid,
(108) 4-[2-(N-benzyl-methylsulfonylamino)-5-trifluoromethylphenoxymethyl]cinnamic acid,
(109) 4-[2-(N-isopropyl-phenylsulfonylamino)-4-trifluoromethylphenoxymethyl]cinnamic acid,
(110) 4-[2-(N-isobutyl-4-ethoxyphenylsulfonylamino)-5-trifluoromethylphenoxymethyl]benzoic acid,
(111) 4-[2-(N-methyl-phenylsulfonylamino)-4-chlorophenoxymethyl]benzoic acid,
(112) 4-[2-(N-cyclopentylmethyl-phenylsulfonylamino)-5-trifluoromethylphenoxymethyl]benzoic acid,
(113) 4-[2-(N-cyclopropylmethyl-phenylsulfonylamino)-5-trifluoromethylphenoxymethyl]benzoic acid,
(114) 4-[2-(N-t-butylmethyl-phenylsulfonylamino)-5-trifluoromethylphenoxymethyl]benzoic acid,

(115) 4-[2-(N-isopropyl-phenylsulfonylamino)-5-trifluoromethylphenoxymethyl]phenylacetic acid,
(116) 4-[2-(N-isopropyl-propylsulfonylamino)-5-trifluoromethylphenoxymethyl]benzoic acid,
(117) 4-[2-(N-isopropyl-pentylsulfonylamino)-5-trifluoromethylphenoxymethyl]benzoic acid,
(118) 4-[2-(N-isopropyl-butylsulfonylamino)-5-trifluoromethylphenoxymethyl]benzoic acid,
(119) 4-[2-(N-isopropyl-hexylsulfonylamino)-5-trifluoromethylphenoxymethyl]benzoic acid,
(120) 4-[2-(N-isopropyl-heptylsulfonylamino)-5-trifluoromethylphenoxymethyl]benzoic acid,
(121) 4-[2-(N-isopropyl-4-hydroxyphenylsulfonylamino)-5-trifluoromethylphenoxymethyl]benzoic acid,
(122) 4-[2-(N-isopropyl-butylsulfonylamino)-5-methylphenoxymethyl]benzoic ecid,
(123) 4-[2-(N-isopropyl-hexylsulfonylamino)-5-methylphenoxymethyl]benzoic acid,
(124) 4-[2-(N-isopropyl-heptylsulfonylamino)-5-methylphenoxymethyl]benzoic acid,
(125) 4-[2-(N-isopropyl-methylsulfonylamino)-5-methylphenoxymethyl]benzoic acid,
(126) 4-[2-(N-isopropyl-ethylsulfonylemino)-5-methylphenoxymethyl]benzoic ecid,
(127) 4-[2-(N-isopropyl-2-phenylethylsulfonylamino)-5-methylphenoxymethyl]benzoic acid,
(128) 4-[2-(N-isopropyl-benzylsulfonylamino)-5-methylphenoxymethyl]benzoic acid,
(129) 4-[2-(N-t-butylmethyl-phenylsulfonylamino)-4-methylphenoxymethyl]benzoic ecid,
(130) 4-[2-(N-isopropyl-methylsulfonylemino)-5-trifluoromethylphenoxymethyl]benzoic acid,
(131) 4-[2-(N-isopropyl-ethylsulfonylamino)-5-trifluoromethylphenoxymethyl]benzoic acid,
(132) 4-[2-(N-isopropyl-cyclopentylmethylsulfonylamino)-5-methylphenoxymethyl]benzoic acid,
(133) 4-[2-(N-cyclohexylmethyl-propylsulfonylemino)-5-methylphenoxymethyl]benzoic ecid,
(134) 4-[2-(N-cyclopentylmethyl-propylsulfonylamino)-5-methylphenoxymethyl]benzoic acid,
(135) 4-[2-(N-isopropyl-propylsulfonylamino)-5-trifluoromethylphenoxymethyl]cinnamic acid,
(136) 4-[2-(N-isopropyl-pentylsulfonylamino)-5-trifluoromethylphenoxymethyl]cinnamic acid,
(137) 4-[2-(N-isopropyl-4-chlorophenylsulfonylemino)-5-trifluoromethylphenoxymethyl]benzoic ecid,
(138) 4-[2-(N-isopropyl-4-ethylphenylsulfonylamino)-5-trifluoromethylphenoxymethyl]benzoic acid,
(139) 4-[2-(N-isopropyl-4-propylphenylsulfonylamino)-5-trifluoromethylphenoxymethyl]benzoic acid,
(140) 4-[2-(N-isopropyl-4-butylphenylsulfonylamino)-5-trifluoromethylphenoxymethyl]benzoic ecid,
(141) 4-(2-phenylsulfonylaminophenoxymethyl)benzoic acid,
(142) 4-[2-(4-chlorophenylsulfonylamino)phenoxymethyl]benzoic acid,
(143) 4-(2-phenylsulfonylamino-4-fluorophenoxymethyl)benzoic acid,
(144) 4-(2-phenylsulfonylamino-5-fluorophenoxymethyl)benzoic ecid,
(145) 4-(2-phenylsulfonylamino-4-bromophenoxymethyl)benzoic acid,
(146) 4-(2-phenylsulfonylamino-5-chlorophenylthiomethyl)benzoic acid,
(147) 4-(2-phenylsulfonylamino-4-methoxyphenoxymethyl)benzoic acid,
(148) 4-(2-phenylsulfonylamino-4-trifluoromethylphenoxymethyl)benzoic ecid,
(149) 4-(2-phenylsulfonylamino-4-methylphenoxymethyl)benzoic ecid,
(150) 4-(2-phenylsulfonylamino-5-methylphenoxymethyl)benzoic acid,
(151) 4-(2-benzylsulfonylemino-5-chlorophenoxymethyl)benzoic ecid,
(152) 4-(2-phenylsulfonylamino-5-methoxyphenoxymethyl)benzoic acid,
(153) 3-(2-phenylsulfonylamino-5-chlorophenoxymethyl)benzoic acid,
(154) 4-(2-phenylsulfonylamino-4-chloro-5-methylphenoxymethyl)benzoic acid,
(155) 4-(2-phenylsulfonylemino-4,5-dichlorophenoxymethyl)benzoic acid,
(156) 4-(2-phenylsulfonylamino-5-chlorophenoxymethyl)phthalic acid,
(157) 4-(2-phenylsulfonylamino-5-chlorophenoxy)benzoic acid,
(158) 4-[3-(2-phenylsulfonylemino-5-chlorophenoxy)propyl]benzoic ecid,
(159) trans-4-(2-phenylsulfonylamino-5-chlorophenoxymethyl)cyclohexanoic acid,
(160) cis-4-(2-phenylsulfonylamino-5-chlorophenoxymethyl)cyclohexanoic acid,
(161) 4-[1RS-(2-phenylsulfonylamino-5-chlorophenoxy)ethyl]benzoic acid,
(162) 4-[2-[N-(2-hydroxy-2-methylpropyl)-phenylsulfonylamino]-5-trifluoromethylphenoxymethyl]benzoic ecid,
(163) 4-[2-[N-(2-hydroxy-2-methylpropyl)-phenylsulfonylamino]-5-trifluoromethylphenoxymethyl]cinnamic acid,
(164) 4-[2-[N-(2-hydroxy-2-methylpropyl)-phenylsulfonylamino]-5-methylphenoxymethyl]benzoic acid,
(165) 4-[2-(N-isopropyl-phenylsulfonylamino)-5-trifluoromethylphenoxymethyl]phenoxyecetic acid,
(166) 4-[2-(N-isopropyl-phenylsulfonylamino)-5-methylphenoxymethyl]phenoxyacetic ecid,
(167) 4-[2-(N-isopropyl-phenylsulfonylamino)-5-methylphenoxymethyl]cinnamic acid,
(168) 4-[2-(N-isopropyl-phenylsulfonylamino)-5-chlorophenoxymethyl]phenoxyacetic acid,
(169) 4-[2-(N-isopropyl-phenylsulfonylamino)-5-chlorophenoxymethyl]cinnamic ecid,
(170) 4-[2-[2-(N-isopropyl-phenylsulfonylamino)-5-trifluoromethylphenoxy]ethyl]benzoic acid,
(171) 2-methoxy-4-[2-(N-isopropyl-phenylsulfonylamino)-5-trifluoromethylphenoxymethyl]benzoic acid,
(172) 2-hydroxy-4-[2-(N-isopropyl-phenylsulfonylamino)-5-trifluoromethylphenoxymethyl]benzoic acid,

(173) 2-hydroxy-4-[2-(N-isopropyl-phenylsulfonylamino)-5-methylphenoxymethyl]benzoic acid,

(174) 2-hydroxy-4-[2-(N-isopropyl-phenylsulfonylamino)-5-chlorophenoxymethyl]benzoic acid,

(175) 4-[2-(N-isopropyl-phenylsulfonylamino)-5-trifluoromethylphenyleminomethyl]benzoic acid,

(176) 4-[N-methyl-[2-(N-isopropyl-phenylsulfonylamino)-5-trifluoromethylphenyl]aminomethyl]benzoic acid,

(177) 4-[2-[N-(1,3-dihydroxyprop-2-yl)-phenylsulfonylamino]-5-trifluoromethylphenoxymethyl]benzoic ecid,

(178) 4-[2-[N-(1,3-dimethoxyprop-2-yl)-phenylsulfonylamino]-5-trifluoromethylphenoxymethyl]benzoic acid,

(179) 4-[2-(N-isopropyl-1-hexenylsulfonylamino)-5-trifluoromethylphenoxymethyl]benzoic acid,

(180) 4-[2-(N-isopropyl-cyclopentylsulfonylamino)-5-trifluoromethylphenoxymethyl]benzoic ecid,

(181) 4-[2-(N-isopropyl-cyclohexylsulfonylamino)-5-trifluoromethylphenoxymethyl]benzoic acid,

(182) 4-[2-(N-isopropyl-cyclohexylsulfonylamino)-5-methylphenoxymethyl]benzoic acid,

(183) 4-[2-(N-isopropyl-isopropylsulfonylamino)-5-trifluoromethylphenoxymethyl]benzoic acid,

(184) 4-[2-(N-isopropyl-isopropylsulfonylamino)-5-methylphenoxymethyl]benzoic acid,

(185) 4-[2-(N-isopropyl-isopropylsulfonylamino)-5-trifluoromethylphenoxymethyl]cinnamic acid.

(186) 4-[2-(N-isopropyl-cyclopentylsulfonylamino)-5-trifluoromethylphenoxymethyl]cinnamic acid.

(187) 4-[2-(N-isopropyl-cyclohexylsulfonylamino)-5-trifluoromethylphenoxymethyl]cinnamic acid.

(188) 4-[2-[N-(N,N-dimathylaminocarbonylmethyl)-phenylsulfonylamino]-5-trifluoromethylphenoxymethyl]benzoic ecid.

(189) 4-(2-phenylsulfonylamino-5-isopropylphenoxymethyl)benzoic acid,

(190) 4-(2-phenylsulfonylamino-5-ethylphenoxymethyl)benzoic acid,

(191) 4-(2-phenylsulfonylamino-5-hydroxymethylphenoxymethyl)benzoic acid,

(192) 4-(2-phenylsulfonyleminomethyl-5-chlorophenoxymethyl)benzoic acid,

(193) 4-[2-(N-isopropyl-phehylsulfonylamino)-5-trifluoromethylphenoxymethyl]phenylpropiolic acid,

(194) 4-(2-phenylsulfonylamino-4-chlorophenoxymethyl)benzyl alcohol,

(195) 4-(2-benzoylamino-5-chlorophenoxymethyl)benzoic acid,

(196) 4-[2-(N-isopropyl-phenylsulfonylamino)-5-isopropylphenoxymethyl]benzoic acid,

(197) 4-[2-(N-methyl-phenylsulfonylemino)-5-isopropylphenoxymethyl]benzoic acid,

(198) 4-(2-(N-isopropyl-phenylsulfonylamino)-5-ethylphenoxymethyl]benzoic acid,

(199) 4-[2-(N-isopropyl-4-propoxyphenylsulfonylamino)-5-trifluoromethylphanoxymethyl]benzoic acid,

(200) 4-[2-(N-isopropyl-4-ethylthiophenylsulfonylamino)-5-trifluoromethylphenoxymethyl]benzoic acid,

(201) 4-[2-(N-isopropyl-4-methylthiophenylsultonylamino)-5-trifluoromethylphenoxymethyl]benzoic acid,

(202) 4-[2-(N-isopropyl-4-butoxyphanylsulfonylamino)-5-trifluoromethylphenoxymethyl]benzoic acid,

(203) 4-[2-(N-isopropyl-4-isopropoxyphenylsultonylamino)-5-trifluoromethylphenoxymethyl]benzoic acid,

(204) 4-[2-(N-isobutyl-benzoylamino)-5-chlorophenoxymathyl]benzoic acid,

(205) 4-[2-(N-isopropyl-benzoylamino)-5-trifluoromethylphenoxymethyl]banzoic ecid,

(206) 6-[2-(N-isopropyl-phenylsulfonylamino)-5-trifluoromethylphenoxymethyl]-2-naphthalic ecid,

(207) 4-[2-(N-isopropyl-butyrylamino)-5-trifluoromethylphenoxymethyl]cinnamic acid,

(208) 4-[2-(N-isopropyl-4-ethoxyphenylsulfonylemino)-5-trifluoromethylphenoxymethyl]cinnamic acid,

(209) 4-[2-(N-isobutyl-4-ethoxyphenylsulfonylamino)-5-trifluoromethylphenoxymethyl]cinnemic acid end

(210) 4-[2-(N-isopropyl-3-ethoxyphenylsulfonylamino)-5-trifluoromethylphenoxymethyl]benzoic acid, end methyl esters thereot.

12. A compound according to claim 1 which is selected trom

(1) 4-[2-[2-(4-chlorophenylsulfonylamino)-5-chlorophenyl]-(E)-vinyl]benzoic acid,

(2) 4-[2-[2-(4-chlorophenylsulfonylamino)-5-chlorophenyl]-(Z)-vinyl]benzoic acid,

(3) 4-[2-[2-(4-chlorophenyl)sulfonylamino-5-chlorophenyl]ethyl]benzoic acid,

(4) 4-[2-[2-(4-chlorophenylsulfonylamino)-5-chlorophenyl]ethynyl]benzoic acid,

(5) 4-[2-[2-(N-isopropyl-phenylsulfonylamino)-5-trifluoromethylphenyl]ethyl]benzoic acid,

(6) 4-[2-[2-(N-isopropyl-phenylsulfonylamino)-5-trifluoromethylphenyl]-(E)-vinyl]benzoic ecid and

(7) 4-[2-[2-(N-isopropyl-phenylsulfonylamino)-5-trifluoromethylphenyl]-(Z)-vinyl]benzoic ecid, and methyl esters thereof.

13. A compound according to claim 1 which is selected from

(1) 4-[2-(N-isopropyl-2-thienylsulfonylamino)-5-chlorophenoxymethyl]benzoic acid,
(2) 4-[2-(N-isopropyl-2-thienylsulfonylamino)-5-methylphenoxymethyl]benzoic acid,
(3) 4-[2-(N-isopropyl-2-furanylsulfonylamino)-5-methylphenoxymethyl]benzoic ecid,
(4) 4-[2-(N-isopropyl-2-furanylsulfonylamino)-5-chlorophenoxymethyl]benzoic acid,
(5) 4-[2-(N-propyl-2-furanylsulfonylamino)-5-trifluoromethylphenoxymethyl]cinnamic acid,
(6) 4-[2-(N-propyl-2-furanylsulfonylamino)-5-methylphenoxymethyl]benzoic acid,
(7) 4-[2-(N-isobutyl-2-furanylsulfonylamino)-5-methylphenoxymethyl]benzoic acid,
(8) 4-[2-(N-isobutyl-2-furanylsulfonylamino)-5-trifluoromethylphenoxymethyl]cinnamic acid,
(9) 4-[2-[N-(prop-2-enyl]-2-furanylsulfonylamino]-5-methylphenoxymethyl]benzoic acid,
(10) 4-[2-[N-(2-methylprop-2-enyl)-2-furanylsulfonylamino]-5-methylphenoxymethyl]benzoic acid,
(11) 4-[2-(N-isobutyl-2-furanylsulfonylamino)-4-methylphenoxymethyl]benzoic acid,
(12) 4-[2-(N-isopropyl-2-furanylsulfonylamino)-4-methylphenoxymethyl]benzoic acid,
(13) 4-[2-[N-(2-methylprop-2-enyl)-2-furenylsulfonylamino]-4-methylphenoxymethyl]benzoic acid.
(14) 4-[2-(N-isopropyl-2-furanylsulfonylamino)-5-methylphenoxymethyl]cinnamic ecid,
(15) 4-[2-(N-isopropyl-2-furanylsulfonylamino)-5-trifluoromethylphenoxymethyl]cinnamic acid,
(16) 4-[2-(N-isopropyl-2-furanylsulfonylamino)-4-trifluoromethylphenoxymethyl]benzoic acid,
(17) 4-[2-(N-isobutyl-2-furanylsulfonylamino)-4-trifluoromethylphenoxymethyl]benzoic acid,
(18) 4-[2-(N-isobutyl-2-furanylsulfonylamino)-5-chlorophenoxymethyl]benzoic acid,
(19) 4-[2-(N-isopropyl-2-furanylsulfonylamino)-5-chlorophenoxymethyl]cinnamic acid,
(20) 4-[2-(N-isobutyl-2-furanylsulfonylamino)-5-chlorophenoxymethyl]cinnamic acid,
(21) 4-[2-(N-isobutyl-2-furanylsulfonylamino)-5-trifluoromethylphenoxymethyl]benzoic acid,
(22) 4-[2-(N-isobutyl-2-furanylsulfonylamino)-4-chlorophenoxymethyl]benzoic acid,
(23) 4-[2-(N-isobutyl-2-furanylsulfonylamino)-4-methylphenoxymethyl]cinnamic acid,
(24) 4-[2-(N-isopropyl-2-furanylsulfonylamino)-5-trifluoromethylphenoxymethyl]benzoic acid,
(25) 4-[2-(N-isopropyl-2-thienylsulfonylamino)-5-trifluoromethylphenoxymethyl]benzoic ecid,
(26) 4-[2-[N-(2-hydroxy-2-methylpropyl)-2-thienylsulfonylamino]-5-trifluoromethylphenoxymethyl]benzoic acid,
(27) 4-[2-(N-isopropyl-2-furoylamino)-5-trifluoromethylphenoxymethyl]benzoic acid,
28) 4-[2-(2-thienylsulfonylamino)-5-chlorobenzoylamino]benzoic acid,
(29) 4-[2-(N-isopropyl-2-furanylsulfonylamino)-5-methylphenylthiomethyl]benzoic acid,
(30) 4-[2-(N-isobutyl-2-thienylsulfonylamino)-5-trifluoromethylphenoxymethyl]cinnemic ecid,
(31) 4-[2-(N-isopropyl-2-furoylamino)-5-trifluoromethylphenoxymethyl]cinnamic acid and
(32) 4-[2-(N-isobutyl-2-furoylemino)-5-trifluoromethylphenoxymethyl]cinnamic acid, and methyl esters thereof.

14. A compound according to claim 1 which is selected from

(1) 5-[2-(N-isopropyl-phenylsulfonylamino)-5-methylphenoxymethyl]furan-2-carboxylic acid,
(2) 6-(2-phenylsulfonylamino-5-chlorophenoxymethyl)nicotinic acid,
(3) 5-[2-(N-isopropyl-phenylsulfonylamino)-5-trifluoromethylphenoxymethyl]thiophene-2-carboxylic acid,
(4) 5-[2-(N-isopropyl-phenylsulfonylamino)-5-trifluoromethylphenoxymethyl]furan-2-carboxylic acid,
(5) 5-[2-(N-isopropyl-phenylsulfonylamino)-5-methylphenoxymethyl]thiophene-2-carboxylic acid,
(6) 5-[2-(N-isopropyl-phenylsulfonylamino)-5-chlorophenoxymethyl]thiophene-2-carboxylic acid,
(7) 5-[2-(N-isopropyl-phenylsulfonylamino)-5-chlorophenoxymethyl]furan-2-carboxylic acid and
(8) 4-(3-phenylsulfonylamino-5-trifluoromethylpyridine-2-yloxymethyl)benzoic acid, and methyl esters thereof.

15. A prostaglandin E_2 antagonist or agonist which comprises the sulfonamide or carboamide derivative of the formula (I) depicted in claim 1 or a non-toxic salt thereof as an active ingredient.

INTERNATIONAL SEARCH REPORT

International application No.
PCT/JP97/04593

A. CLASSIFICATION OF SUBJECT MATTER
Int.Cl⁶ C07C233/25, 233/75, 237/42, 311/13, 311/21, 311/17, 311/29, C07D213/76, 213/80, 307/42, 307/64, 307/68, 333/34, 333/40,
According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
Int.Cl⁶ C07D233/25, 233/75, 237/42, 311/13, 311/21, 311/17, 311/29, C07D213/76, 213/80, 307/42, 307/64, 307/68, 333/34, 333/40,

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)
CAS ONLINE

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	JP, 4-308560, A (Eli Lilly and Co.), October 30, 1992 (30. 10. 92) & EP, 491525, A1 & US, 5397798, A	1-15
A	JP, 2-72150, A (Otsuka Pharmaceutical Factory, Inc.), March 12, 1990 (12. 03. 90) (Family: none)	1-15
A	JP, 59-16871, A (Shionogi & Co., Ltd.), January 28, 1984 (28. 01. 84) (Family: none)	1-15

☐ Further documents are listed in the continuation of Box C ☐ See patent family annex.

* Special categories of cited documents:
"A" document defining the general state of the art which is not considered to be of particular relevance
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"P" document published prior to the international filing date but later than the priority date claimed
"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art
"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
March 11, 1998 (11. 03. 98)	March 24, 1998 (24. 03. 98)
Name and mailing address of the ISA/ Japanese Patent Office	Authorized officer
Facsimile No.	Telephone No.

Form PCT/ISA/210 (second sheet) (July 1992)

INTERNATIONAL SEARCH REPORT

International application No.
PCT/JP97/04593

A. (Continuation) CLASSIFICATION OF SUBJECT MATTER

A61K31/195, 31/24, 31/245, 31/34, 31/38

B. (Continuation) FIELDS SEARCHED

A61K31/195, 31/24, 31/245, 31/34, 31/38

Form PCT/ISA/210 (extra sheet) (July 1992)